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James R. Howe
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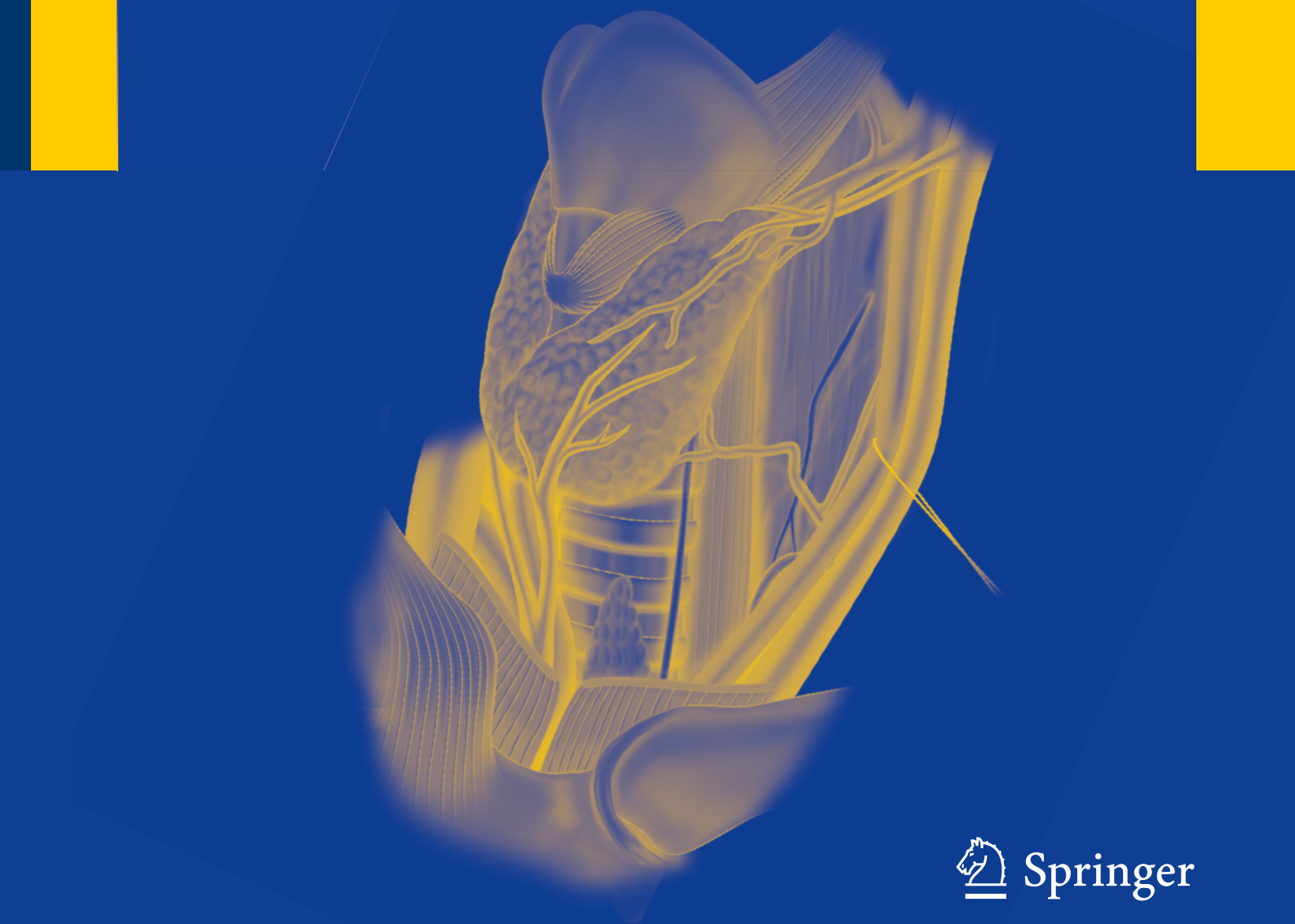
Endocrine and Neuroendocrine Surgery



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Endocrine and Neuroendocrine Surgery

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Springer Surgery Atlas Series
ISBN 978-3-662-54065-7 ISBN 978-3-662-54067-1 (eBook)
DOI 10.1007/978-3-662-54067-1

Library of Congress Control Number: 2017940482

Printed on acid-free paper

This Springer imprint is published by Springer Nature
The registered company is Springer-Verlag GmbH Germany
The registered company address is: Heidelberger Platz 3, 14197 Berlin, Germany

Preface

Although tumors of the endocrine system have challenged physicians since ancient times, our understanding of these disorders has made rapid progress over the past century. Identification of the parathyroid glands in 1880 by Ivar Sandstrom, Theodor Kocher's Nobel Prize in 1909 for his work on the pathophysiology of the thyroid gland and safe surgery, and Cushing's work on pituitary tumors are several notable examples. These tumors are unique from other solid tumors in that they may be benign or malignant, yet cause clinical syndromes due to excess secretion of hormones. Other tumors from the endocrine system may be nonfunctional and malignant, such as thyroid tumors, or incidentally discovered during workup for other conditions.

Neuroendocrine tumors are comparable to their endocrine counterparts in that they frequently also secrete hormones that give rise to symptoms. We have also come a long way in our understanding of neuroendocrine tumors over the past century. Ransom's account of a patient with an ileal tumor, liver metastases, and diarrhea in 1890, Oberndorfer's description of ileal tumors as "karzinoide" in 1907, and Pearse's depiction of the diffuse amine precursor uptake and decarboxylase system in 1969 are just a few of the important observations. These tumors continue to present challenges due to their frequent diagnosis at advanced stages, making their management complex.

Surgeons treating endocrine and neuroendocrine neoplasms must be knowledgeable about their respective pathophysiology, in order to select appropriate imaging and biochemical tests to make the diagnosis and localize the tumor. They must also be familiar with the expected patterns of local, regional, and distant tumor spread in order to best effect cure or palliation. And finally, they should be proficient with the anatomic challenges presented by the many regions of the body where these tumors may arise.

There is a wealth of authoritative texts and atlases on the subject of endocrine surgery, but very few are also devoted to neuroendocrine tumors. The rising incidence of these cancers has led the general surgeon to encounter them with increasing frequency, but their management is not as well understood as endocrine tumors. For detailed descriptions of pathophysiology and diagnostic workup, we direct readers to the textbooks focusing upon these specific topics.

The objective of this book is to comprehensively describe the surgical approaches to endocrine and neuroendocrine tumors. To do this, I have gathered together a group of talented surgeons who I have had either the honor of working with or getting to know over the past few decades, who represent some of the most talented figures on these subjects in the field of surgery. Here the focus is upon the selection of patients for operation and detailed descriptions of these operative techniques. These are exhibited through beautiful color illustrations and concise text, and it is my hope that these chapters will enhance the delivery of excellent care from residents, fellows, and practicing clinicians to their patients with these tumors.

Iowa City, IA, USA — James R. Howe

Acknowledgments

This book is dedicated to my wife, Denise, for her patience over the years as I trained and later practiced in the art of surgery. It simply would not have been possible without her loving support and the many sacrifices she made over the years for our family. I would also like to thank Ron Weigel for his guidance over the past decade as my Chairman, Carol Scott-Conner, for giving me my first academic opportunity, and Sam Wells and Murray Brennan for their incomparable training and mentorship. I also extend my sincere appreciation to all of the authors who contributed their time and expertise, and especially to my friend James Mezhir, who could not be with us in this satisfying moment. Finally, I commend Lee Klein for his skill in shepherding this volume from just an idea through to its actual creation.

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Part I

Parathyroid

Radioguided Parathyroidectomy

1

Herbert Chen

1.1 Introduction

Surgery is the only curative treatment for primary hyperparathyroidism. Several intraoperative adjuncts have been developed to facilitate parathyroidectomy to achieve a successful outcome. These include sestamibi-SPECT scanning, cervical ultrasound, 4D-CT scans, and intraoperative parathyroid hormone monitoring. One technology often overlooked is radioguided parathyroidectomy.

Radioguided parathyroidectomy is closely related to other radioguided techniques already in use for breast cancer, malignant melanoma, thyroid cancer, and colon cancer. A radiotracer is administered, which accumulates preferentially in the targeted tissue. Radioguided techniques localize specific tissue through the use of radioactivity, theoretically minimizing dissection and decreasing overall operative time.

The radiotracer utilized for radioguided parathyroidectomy is technetium ^{99m}Tc–sestamibi, which is the same compound used for preoperative parathyroid imaging. Its use is based upon the principle that enlarged, hypercellular parathyroid glands contain an increased number of mitochondria, and these mitochondria take up and retain ^{99m}Tc–sestamibi longer than surrounding tissues. Thus, the abnormal parathyroid becomes "hot" relative to surrounding structures. A hand-held gamma probe can then be utilized to detect the enlarged parathyroid gland. Once resected, the parathyroid gland can be assessed ex vivo for its radioguided counts. The counts are then used to determine if the gland is abnormal.

Radioguided parathyroidectomy has been shown to be effective in patients with primary, secondary, and tertiary hyperparathyroidism. It is not limited to patients who have positive sestamibi scans; it can also be used in those with negative scans. Thus, this technology is applicable to all patients undergoing surgery for hyperparathyroidism. The following sections discuss the details of the technique and its advantages.

1.2 Technique

About 1 hr prior to surgery, patients undergo an intravenous injection of 10 mCi ^{99m}Tc–sestamibi, one half the dose used for SPECT imaging (the effective time range can be from 20 min to 6 hr). We generally do not obtain any imaging on the day of surgery. Patients are then transported to the operating room for the procedure.

Once in the operating room, the patient is positioned in a beach chair orientation. At our institution, we routinely use general anesthesia with either an endotracheal tube or a laryngeal mask airway, but the procedure also can be performed under local anesthesia with monitored anesthesia care. Intraoperative parathyroid hormone (PTH) monitoring is utilized at our institution for virtually all parathyroidectomies. We draw a baseline PTH level after induction of anesthesia. The incision is generally 1.5–3.0 cm in length, and is made along a skin crease centered over the midline (Fig. 1.1). In cases of reoperative surgery, we try to use part of the old incision but occasionally may make a lateral incision along the anterior border of the sternocleidomastoid muscle for an upper parathyroid adenoma. Prior to incision, a background radioactivity count is performed. We obtain the background counts by placing the gamma probe over the thyroid isthmus (Fig. 1.2). However, other parathyroid surgeons prefer to obtain the background count over the left shoulder. We use an 11-mm collimated gamma probe (Neoprobe® 2000, Ethicon Endo-Surgery, Cincinnati, OH).

Once the background count has been obtained, the incision is made (Fig. 1.3). The subcutaneous tissues and platysma are divided horizontally without making skin flaps, and the strap muscles are divided vertically in the midline (Figs. 1.4 and 1.5). Many times, a preoperative localization scan will identify the location of the abnormal parathyroid

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J.R. Howe (ed.), *Endocrine and Neuroendocrine Surgery*, Springer Surgery Atlas Series, DOI 10.1007/978-3-662-54067-1_1

gland and guide a focused approach. In those cases, the probe does not really add much more information about the location of the abnormal parathyroid. In cases of negative sestamibi scans, or if a bilateral exploration is planned, the gamma probe can be inserted through the incision to aid in identifying the location of abnormal parathyroid glands. The probe can be directed behind the thyroid gland to localize the parathyroid gland. Hypercellular parathyroid glands have in vivo radioactive counts higher than the background counts (Fig. 1.6). The probe in these cases can direct the area to dissect. After dissecting out the abnormal parathyroid gland, the vascular pedicle is clipped and divided (Fig. 1.7). The resected parathyroid gland is then placed on top of the gamma probe to obtain ex vivo counts (Fig. 1.8). Radioactive counts at least 20% of background have been shown to be consistent with hyperfunctioning parathyroid tissue, confirming successful resection of an abnormal gland. Lymph nodes, fat, and normal parathyroid tissue have been shown to have radioactive counts less than 20% of background.

We then sample for intraoperative parathyroid hormone (PTH) levels at 5, 10, and 15 min after resection of the parathyroid gland. If the PTH levels fall by more than 50%, the

Figure 1.1

Incision placement

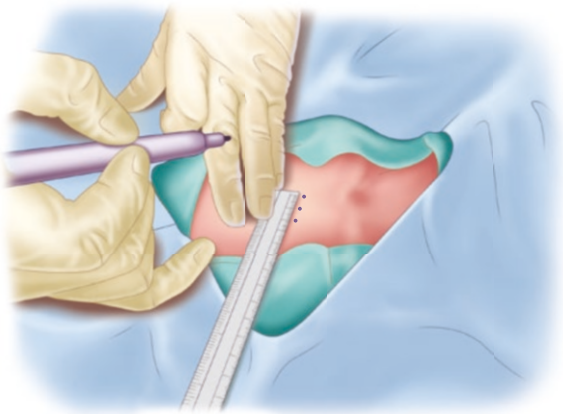
Figure 1.2

The background radioactivity count level can be obtained by placing the gamma probe over the thyroid isthmus

operation is terminated. If the levels do not fall, further exploration is continued until other abnormal parathyroid glands are identified and resected. Once the operation is complete, the strap muscles are closed with a running 2-0 Vicryl suture. The wound is then injected with 20 mL 0.25% Marcaine (Fig. 1.9). The platysma is closed with a running 3-0 Vicryl suture. The skin is closed with a 5-0 Prolene subcuticular closure or skin glue (Fig. 1.10).

After surgery, patients are observed for a few hours in the same-day surgery unit. Nearly all patients are discharged home the same day as surgery. Ice packs are routinely used at our institution to minimize tissue swelling and aid in pain control. Oral analgesics are generally all that is needed to achieve adequate pain control. Patients are discharged home on oral TUMS® (GlaxoSmithKline) or other forms of calcium for 1 week to treat potential postoperative hypocalcemia due to bone hunger, and they are instructed to take additional doses for any symptoms of hypocalcemia (numbness, tingling, cramping). No labs are drawn until the postoperative visit 1 week later. Calcium and PTH levels are drawn at the 1-week and 6-month postoperative visits.

Figure 1.1



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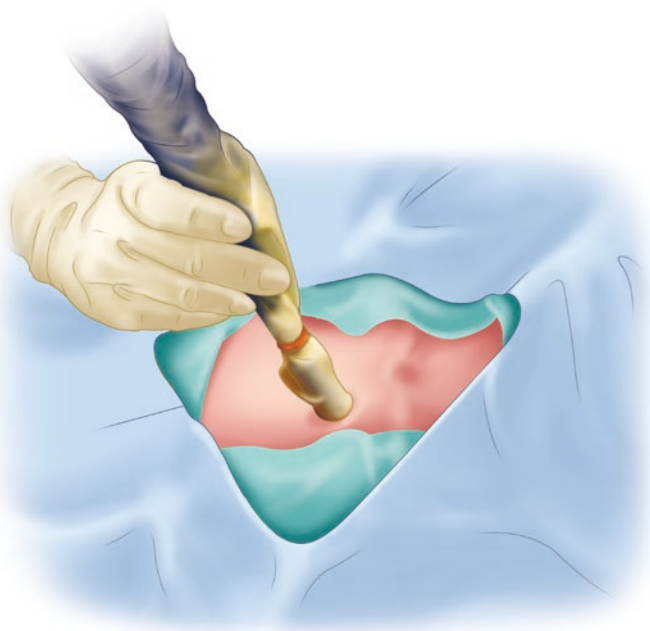


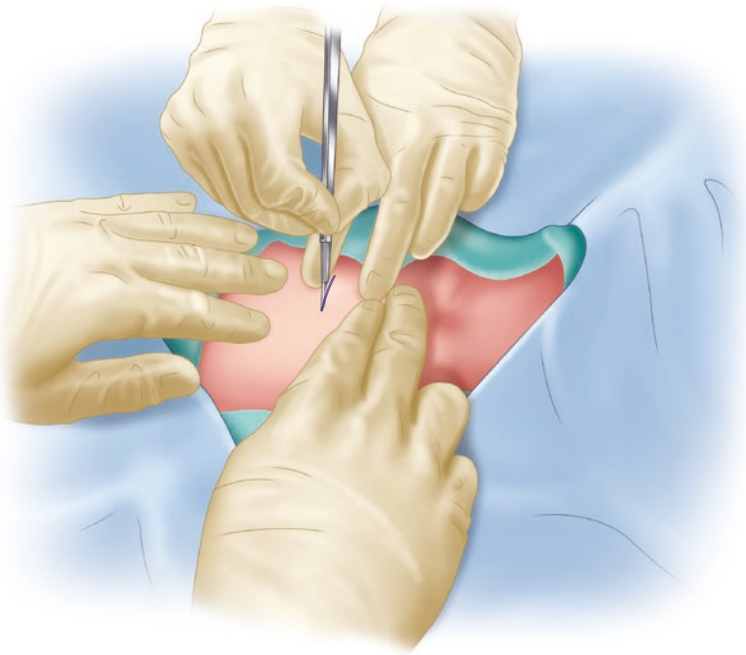
Figure 1.3

Making the incision

Figure 1.4

Dividing the platysma

Figure 1.3



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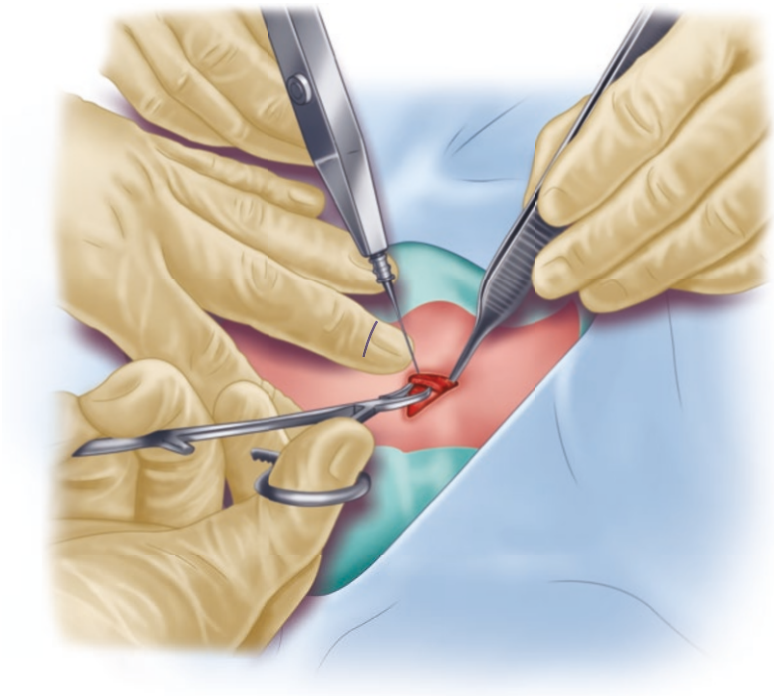


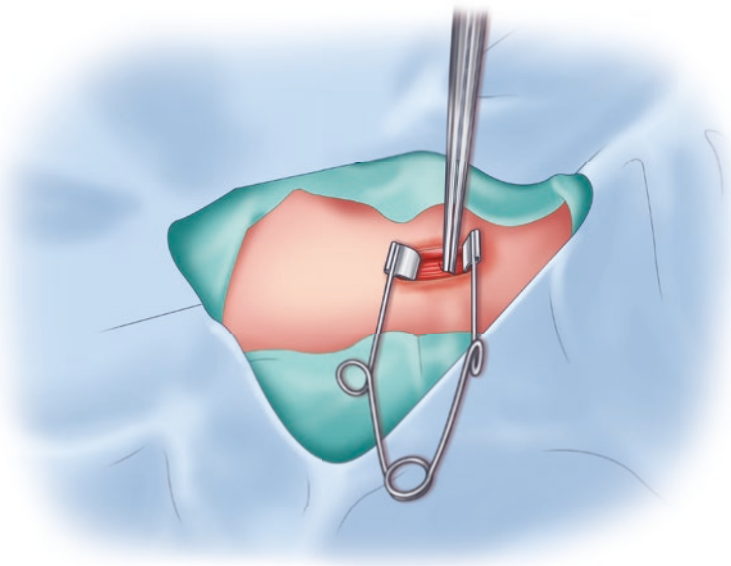
Figure 1.5

Dividing the strap muscles in the midline

Figure 1.6

Identifying the abnormal parathyroid gland with the gamma probe

Figure 1.5



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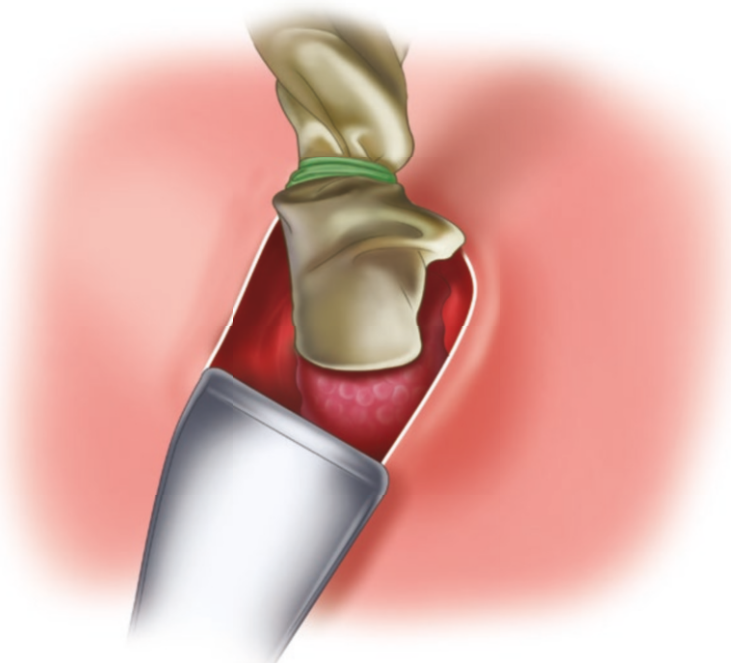


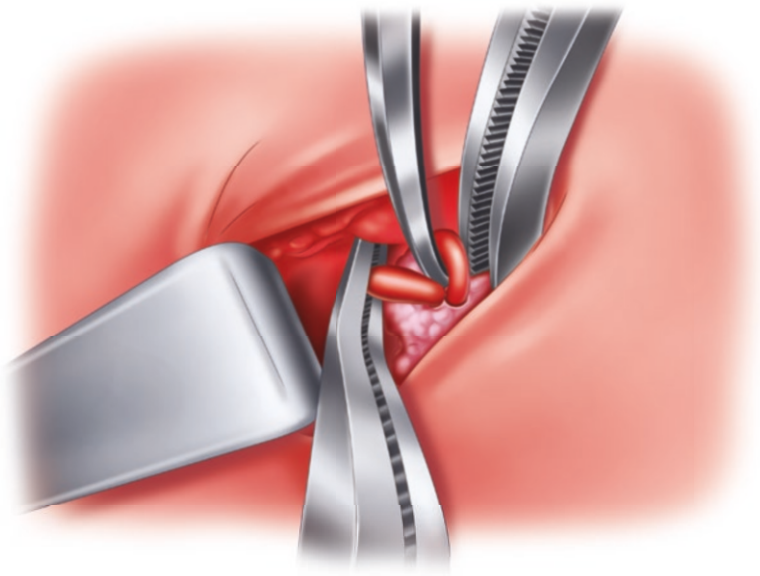
Figure 1.7

Isolating the vascular pedicle

Figure 1.8

Measuring ex vivo radioactive counts from the resected parathyroid gland

Figure 1.7



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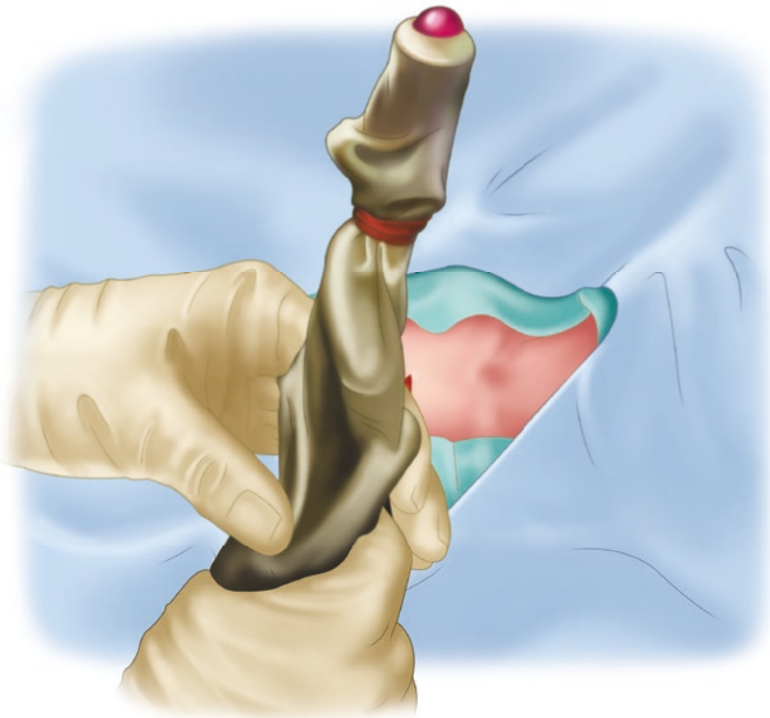


Figure 1.9

Injecting local anesthetic in the wound

Figure 1.10

Subcuticular closure

Figure 1.9

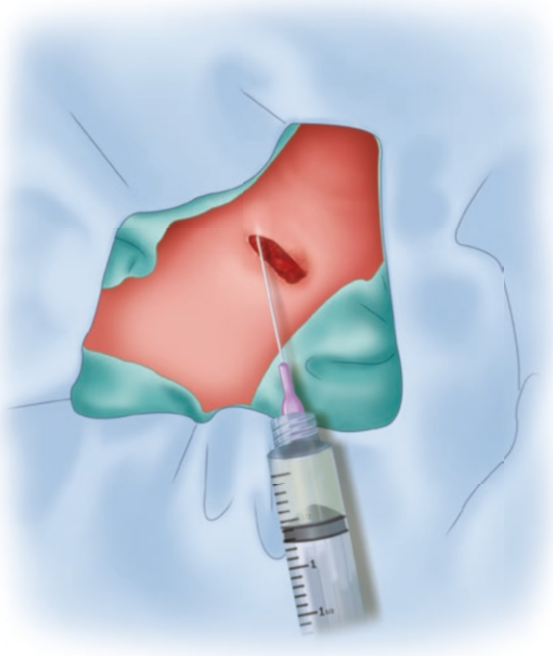
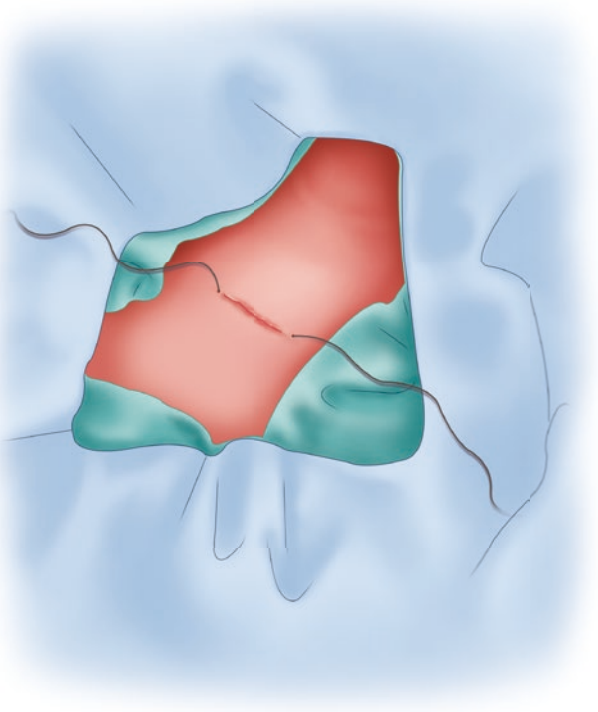


Figure 1.10



1.3 Discussion

Radioguided parathyroidectomy is another potential tool at the disposal of parathyroid surgeons. Because all hospitals often use the technology for sentinel node biopsies, radioguided parathyroidectomy is available to most surgeons. Although we use the Neoprobe® for our procedures, we have had experience with other hand-held probes, and all were sensitive for the detection of hypercellular parathyroids. We and others have previously shown that radioguided techniques are useful in patients with primary, secondary, or tertiary hyperparathyroidism. Furthermore, radioguided parathyroidectomy is effective in many special circumstances.

1.3.1 Sestamibi-Negative Patients

The gamma probe is able to detect high radioactive counts from all enlarged, hyperfunctioning parathyroid glands, including those that do not appear on imaging studies. Parathyroid localization studies such as sestamibi-SPECT, cervical ultrasound, and CT scans will fail to localize an abnormal parathyroid gland in up to 20% of patients with primary hyperparathyroidism. These glands tend to be smaller. Because the gamma probe can be positioned very close to the parathyroid, it can detect radioactive counts with great sensitivity. Abnormal parathyroid glands missed on imaging studies will still take up sestamibi at higher levels than surrounding tissue.

1.3.2 Ectopic Glands

The gamma probe can be helpful in localizing abnormal parathyroid glands in ectopic locations, such as intrathyroidal, undescended, and mediastinal glands. If a preoperative sestamibi scan shows a parathyroid adenoma down in the mediastinum, a video-assessed thoracoscopic approach with a laparoscopic gamma probe can be used.

1.3.3 Familial Primary Hyperparathyroidism

We have shown that radioguided parathyroidectomy is very effective in patients with familial primary hyperparathyroidism, parathyroid hyperplasia, or both. Though parathyroid adenomas tend to have ex vivo counts well over 20% of background, patients with parathyroid hyperplasia from primary hyperparathyroidism tend to have ex vivo counts between 20% and 40%.

1.3.4 Secondary and Tertiary Hyperparathyroidism

Patients with secondary or tertiary hyperparathyroidism most commonly have parathyroid hyperplasia. We do not routinely obtain preoperative imaging studies in these patients at their initial parathyroidectomy and perform bilateral exploration. We have shown that radioguided parathyroidectomy may reduce operative time in these patients. In patients with previous autotransplants, the gamma probe can localize the hyperplastic parathyroid tissue within the muscle body. To minimize confusing background levels, the sestamibi injection should be administered in the contralateral limb of these patients.

1.3.5 Pediatric Patients

Radioguided parathyroidectomy is safe and effective for children with hyperparathyroidism. The same dose of ^{99m}Tc–sestamibi can be administered.

1.3.6 Reoperative Surgery

Many surgeons believe that radioguided techniques do not provide much additional information for patients undergoing an initial operation for hyperparathyroidism, but most acknowledge that this technology has an important role in reoperative parathyroidectomy. During these potentially difficult operations, scar tissue can obscure landmarks, making identification of the abnormal parathyroid challenging. The gamma probe in these circumstances can facilitate intraoperative localization (through high in vivo radioactive counts) and can confirm successful resection of hyperfunctioning parathyroid tissue (by high ex vivo radioactive counts).

1.4 Summary

Radioguided parathyroidectomy is an underappreciated technique for the management of patients with primary, secondary, or tertiary hyperparathyroidism. It should be considered as part of the surgical armamentarium for patients undergoing parathyroidectomy.

Suggested Reading

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Minimally Invasive Parathyroidectomy with Intraoperative PTH Testing

2

Ronald J. Weigel

2.1 Introduction

Primary hyperparathyroidism results from the growth and enlargement of one or more parathyroid glands. In approximately 85% of patients, a single adenoma is identified, whereas approximately 15% of patients present with multigland disease. Patients with multigland disease often have asymmetric enlargement with involvement of two, three, or all four parathyroid glands. Surgical resection remains the mainstay of treatment for primary hyperparathyroidism.

The classic surgical treatment for primary hyperparathyroidism is neck exploration with identification of all four parathyroid glands, resection of the enlarged gland or glands, and biopsy of normal glands [1]. This operative approach has extremely high cure rates, with the incidence of persistent or recurrent hyperparathyroidism in the range of 2% in the hands of an experienced parathyroid surgeon. Complications, including nerve injury and neck hematoma, are uncommon and occur in less than 1% of patients.

Given the high success rate and low complication rate for the classic operation for hyperparathyroidism, surgeons have been challenged to introduce modifications that further improve the operation while maintaining high success rates. It should be noted, however, that the classic four-gland exploration may often result in extended operations, with the identification of all normal parathyroid glands requiring additional anesthesia and operative time, yet with little benefit to the patient. In addition, routine four-gland exploration exposes the patient to the potential of nerve injury on a side of the neck that may not require exploration. Several improvements in technology have offered the potential of minimally invasive parathyroidectomy (MIP). The definition of MIP covers several modifications, but it commonly indicates an open operative procedure to remove a parathyroid adenoma through an incision less than 3–4 cm in length, without routine identification of the normal glands [2].

Several technological advances have allowed MIP to be performed safely with excellent outcomes. The first development was the rapid intraoperative parathyroid hormone (IOPTH) assay, which allowed the surgeon to document an appropriate fall in the PTH level after successful removal of the parathyroid adenoma responsible for primary hyperparathyroidism [3]. The second technological advance was the improvement of imaging techniques, which allowed accurate localization and a directed operation [4]. Failure to successfully localize a parathyroid adenoma preoperatively creates a clinical situation in which the surgeon must rely on a classic bilateral neck exploration to identify and resect the abnormal parathyroid gland(s). The IOPTH assay can also be used in this situation to help ensure successful resection of all abnormal parathyroid glands.

2.2 Technique

2.2.1 Preoperative Imaging

The surgical approach for MIP is influenced by the preoperative imaging, patient habitus, and additional medical concerns specific to the given patient. For example, local anesthesia can be used quite successfully for patients with medical conditions in which general anesthesia should be avoided [2]. In addition, if preoperative imaging indicates enlargement of an inferior gland, which is often more anterior, the gland can be approached through a smaller incision than would be needed for a superior gland, whose posterior position often requires a deeper dissection and thus may require a larger incision to expose the important anatomic structures safely. In the example shown in Fig. 2.1a, evaluation of imaging prior to MIP is critical. In this example, ultrasound demonstrated a normal thyroid with a likely parathyroid adenoma in the left inferior gland position

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J.R. Howe (ed.), *Endocrine and Neuroendocrine Surgery*, Springer Surgery Atlas Series, DOI 10.1007/978-3-662-54067-1_2

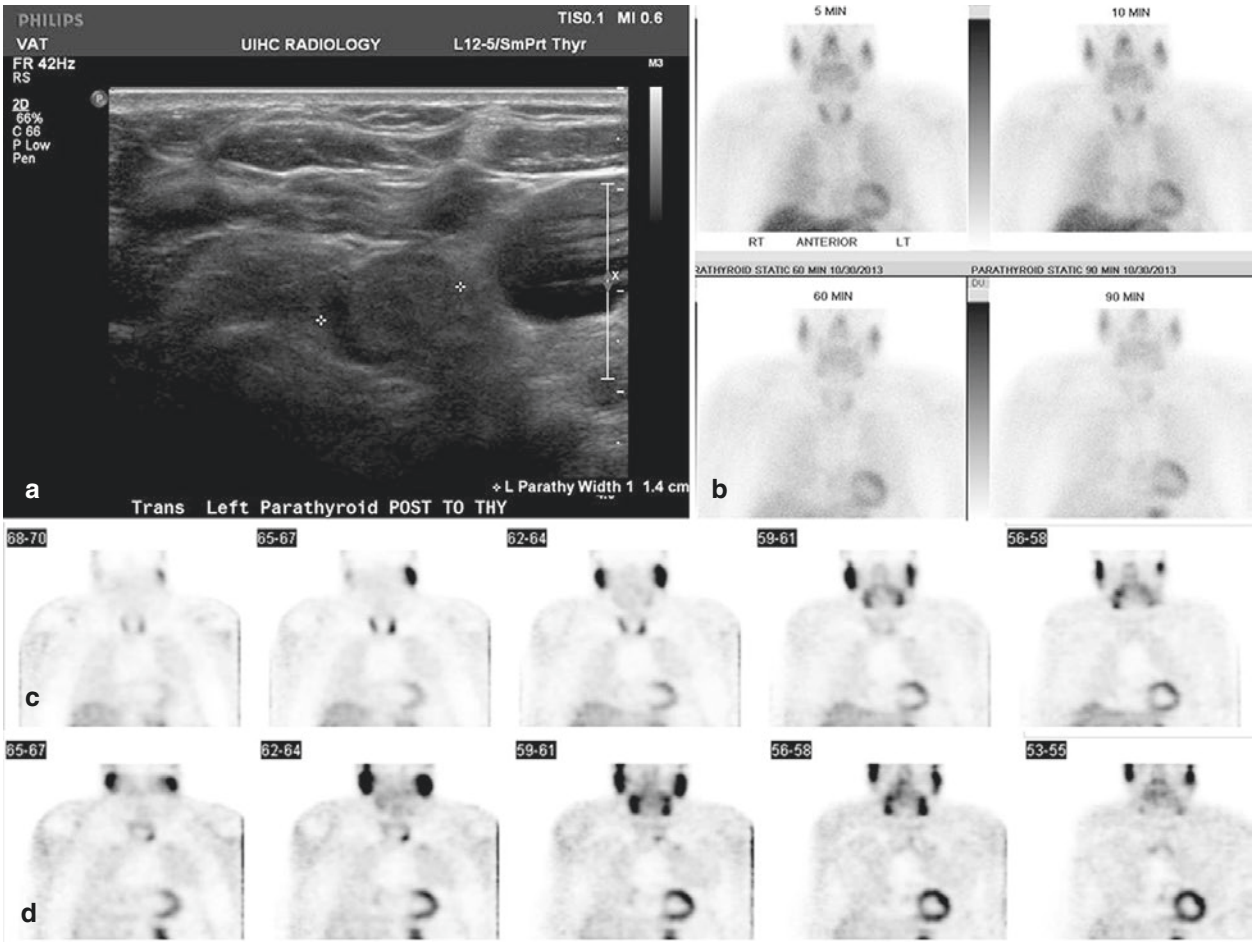
(Fig. 2.1a). The adenoma can be seen lying medial and posterior to the left carotid artery in close proximity to the inferior pole of the left thyroid lobe. A sestamibi scan similarly identified a parathyroid adenoma in the left inferior gland position. Although planar images demonstrated questionable findings (Fig. 2.1b), SPECT imaging is a refinement that allows better anatomic localization on sestamibi, demonstrating an anteriorly placed parathyroid adenoma in the left inferior gland position (Fig. 2.1c, d). As shown, thyroid uptake is normally more intense on the early images (Fig.

Figure 2.1

Preoperative imaging in a patient with primary hyperparathyroidism. (**a**) High-resolution ultrasound identified a likely parathyroid adenoma between the left thyroid lobe and the left carotid artery. (**b**) Planar images from a sestamibi scan fail to convincingly localize a parathyroid adenoma. (**c**) SPECT-sestamibi images from the same patient at 15 min suggest a left lower parathyroid adenoma and agree with the ultrasound findings in (**a**). (**d**) Delayed SPECT-sestamibi images at 90 min show washout in the thyroid and enhancement of the parathyroid adenoma, convincingly localizing a left inferior parathyroid adenoma

2.1c), but it washes out, leading to greater relative intensity of uptake in the parathyroid adenoma on delayed images (Fig. 2.1d). The agreement between ultrasound and sestamibi is highly suggestive of single-gland disease and the patient can most likely undergo a successful parathyroidectomy using the MIP approach [4].

Figure 2.1



2.2.2 Surgical Procedures

After the patient's identity is confirmed and the operative site is marked, the patient is brought to the operating room. Most often, the procedure is done under general anesthesia, which results in patient comfort and an overall shorter operative procedure. After the induction of adequate general anesthesia, the patient is positioned with a roll behind the shoulders, with the neck in slight extension (Fig. 2.2). The arms should be tucked, allowing better access to the neck and shoulder area during the surgical procedure. A small transverse incision of approximately 2–3 cm is made sharply with a scalpel. The electrocautery setting should be at pure cut, at the lowest setting that allows efficient transection of tissues. Using electrocautery, dissection is carried down through the platysma muscle while avoiding transection or injury of deeper structures (Fig. 2.3). Using skin hooks to elevate the skin, a subplatysmal flap is developed, leaving the anterior jugular veins, strap muscles, and sternocleidomastoid muscles undisturbed. The platysma and subcutaneous tissue are retracted with a self-retaining retractor. The strap muscles are divided at the midline, exposing the thyroid lobe on the side where the adenoma was localized (Fig. 2.4). Retraction of the strap muscles is performed and dissection is carried out to mobilize the strap muscles off the mid-neck structures. A Babcock clamp is placed on the thyroid lobe after division of the middle thyroid vein, mobilizing the thyroid up into the incision (Figs. 2.5 and 2.6). Retraction of the thyroid allows for better exposure of the deeper structures and often helps mobilize the parathyroid gland up into the incision (Figs. 2.5

Figure 2.2

Positioning a patient for minimally invasive parathyroidectomy (MIP). The patient is positioned with a roll behind the shoulders to place the head in slight extension. A 2- to 3-cm incision is made approximately 1–2 cm above the sternal notch

and 2.6b). The carotid artery should be identified by palpation but is not necessarily exposed. An appendiceal or lateral retractor is used to retract the carotid artery laterally, opening up the mid-neck space.

Anatomic dissection within the mid-neck space is directed by the preoperative imaging. An inferior parathyroid gland is usually found anterior and medial to the course of the recurrent laryngeal nerve and lateral or inferior to the edge of the thyroid. A superior parathyroid gland is often further posterior, and is most commonly superior and slightly lateral to the course of the recurrent nerve. Often the nerve is identified and exposed during the course of the dissection. Care should be taken to move neck structures away from the nerve, to leave the nerve undisturbed and along its normal course in the neck. Some surgeons employ nerve monitoring, but the routine use of nerve monitoring has not been shown to decrease the nerve injury rate [5]. The parathyroid adenoma, once identified, is mobilized using sharp and blunt dissection. Fibrous attachments are cut using monopolar electrocautery. The gland should be mobilized until it is attached by its pedicle. The pedicle is clamped, transected, and ligated with a 3-0 silk suture. The parathyroid adenoma is sent to pathology and frozen section is used to confirm the presence of hypercellular parathyroid tissue. Surgeons often omit the frozen section step, but ectopic thyroid tissue or enlarged lymph nodes could potentially be resected inadvertently, and frozen section can help to ensure that the parathyroid adenoma was removed.

Figure 2.2

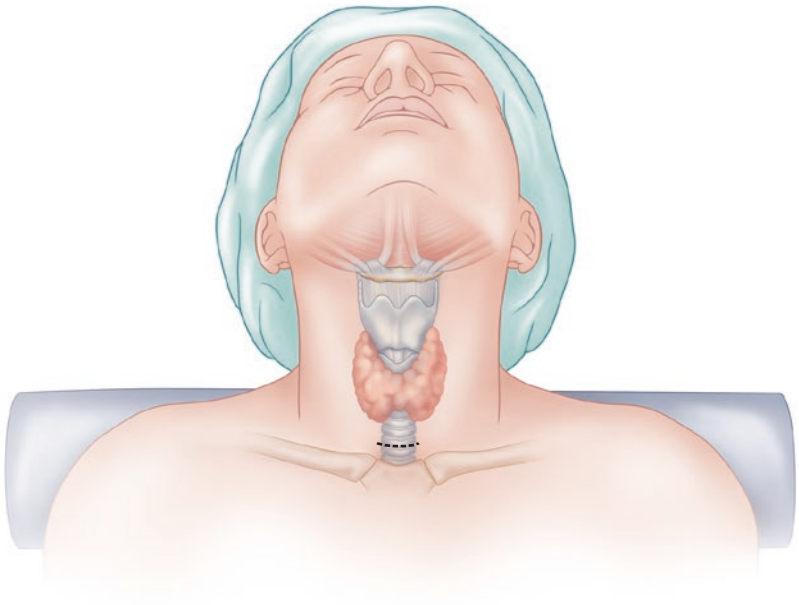


Figure 2.3

Developing a subplatysmal plane. The skin and subcutaneous tissue are retracted using skin hooks. Using electrocautery, the platysma is dissected off the strap muscles. After developing a superior and inferior flap, the platysma is retracted with a self-retaining retractor

Figure 2.4

Mobilization of the strap muscles. The strap muscles are mobilized off the mid-neck structures, exposing the thyroid lobe on the side localized by preoperative imaging.

Figure 2.3

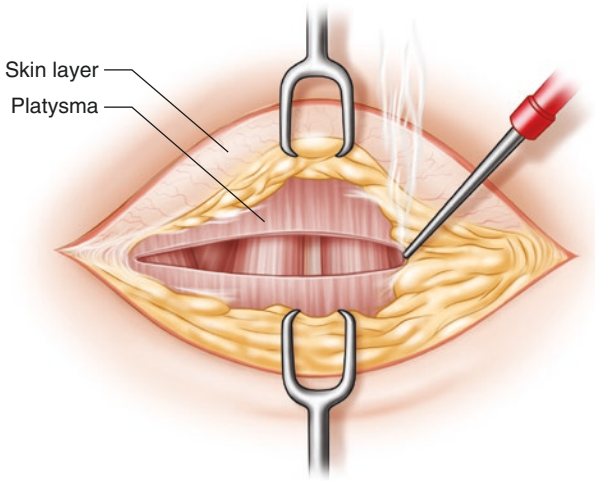


Figure 2.4

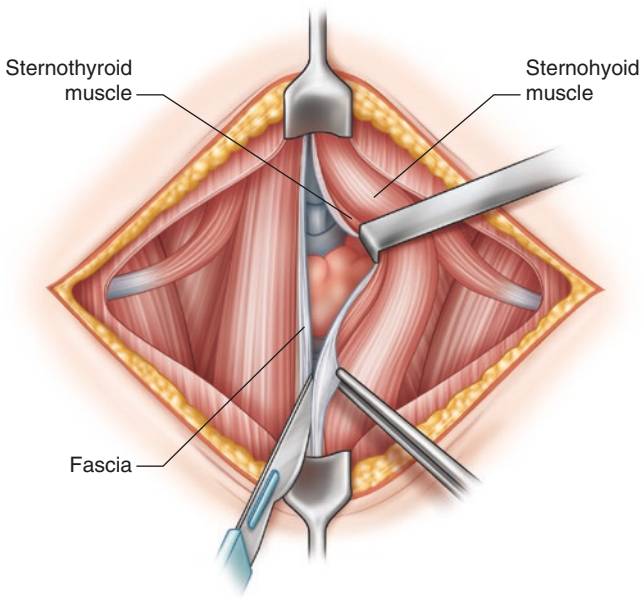


Figure 2.5

Mobilization of the thyroid and resection of the parathyroid adenoma. The thyroid lobe is retracted into the incision, exposing the deeper mid-neck structures. The parathyroid adenoma is identified by sharp and blunt dissection in the mid-neck space. The adenoma is mobilized and resected

Figure 2.6

Example of an MIP operation. These operative photographs show successful MIP in the patient whose preoperative localization studies are shown in Fig. 2.1. (**a**) After retraction of the strap muscles, the left mid-neck structures are exposed and the parathyroid adenoma is identified. (**b**) The parathyroid adenoma is being mobilized. (**c**) The adenoma is resected; a Babcock clamp is seen on the thyroid lobe. (**d**) The incision is closed, completing successful MIP via an incision slightly less than 3 cm. The baseline intraoperative parathyroid hormone (IOPTH) in this patient at the time of neck incision was 137 pg/mL. The level 10 min after the adenoma was resected completely (**c**) was 31 pg/mL

Figure 2.5

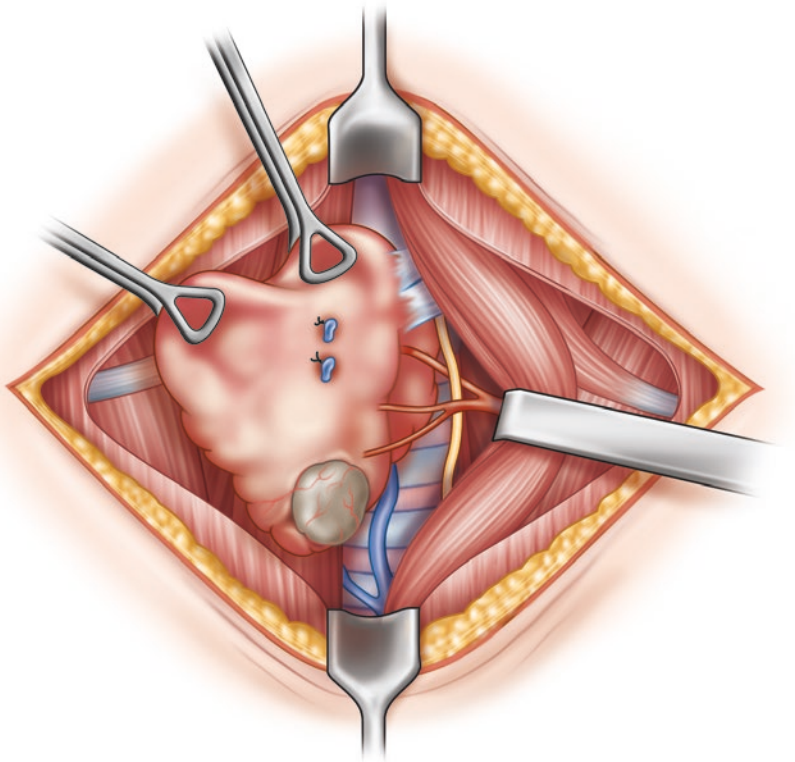
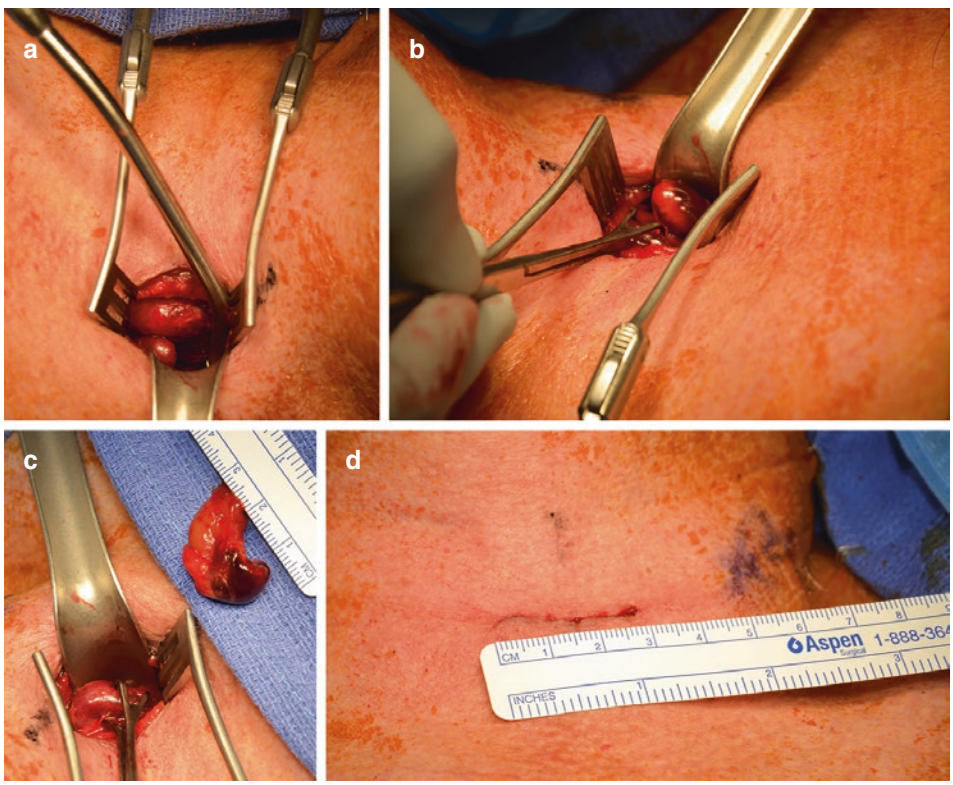


Figure 2.6



2.2.3 Measurement of PTH Levels

The IOPTH should be used during MIP. The first level should be drawn at approximately the time of neck incision. It is best to use a peripheral vein, as levels measured within the neck can be influenced by the anatomic location of the adenoma. A second level is taken at the time that the adenoma is resected. This is considered "time zero." A spike in PTH level can occur with mobilization of an adenoma, so the level at time zero should be the highest possible peak from which an appropriate drop in PTH can be measured after resection [6]. A third PTH level is measured approximately 10 min after time zero. Most often, surgical closure is being performed while waiting for the PTH levels. A minimum of a 50% fall in the PTH level should be anticipated for a successful parathyroidectomy, and the level in most cases should fall into the normal range, though there is evidence that a normal level is not necessary to indicate successful parathyroidectomy [7]. Another consideration at the time of surgery is the potential identification of the normal parathyroid gland on the ipsilateral side. Identification of a normal parathyroid gland, which can be confirmed by biopsy, further supports single-gland disease.

2.2.4 Closure and Postoperative Care

After parathyroidectomy, the strap muscles are reapproximated in the midline with interrupted 3-0 Vicryl sutures. The platysma is similarly reapproximated, and the skin is closed with a running 4-0 monocryl suture, resulting in a cosmetically excellent result (Fig. 2.6d). Steri-strips or surgical glue are applied and the operation is terminated. Postoperative management involves watching the patient for approximately 4 hr, assessing the patient for normal voice, and confirming that there is no evidence of bleeding. The patient should take calcium supplementation postoperatively and return to the clinic in 1–2 weeks, at which time calcium and PTH levels should be evaluated.

2.3 Discussion

MIP has become the standard of care for most patients who present with primary hyperparathyroidism. Preoperative localization with ultrasound and/or sestamibi scan is necessary to successfully use this approach. IOPTH monitoring helps to ensure that removal of a single adenoma is likely to result in a cure of primary hyperparathyroidism.

2.3.1 Complex Findings on Preoperative Imaging

Several features of preoperative imaging can alter the anticipated approach for MIP. One finding on preoperative imaging is the identification of a concomitant thyroid nodule on ultrasound. Based on size and imaging characteristics, many thyroid nodules should be evaluated by fine-needle aspiration prior to neck exploration. The identification of a papillary thyroid cancer or other thyroid disease necessitating thyroidectomy precludes the MIP approach, as these patients should undergo thyroidectomy at the time of neck exploration. Another common finding is discordant imaging, in which either ultrasound or sestamibi scan identifies an abnormality consistent with an adenoma, but the other imaging modality fails to agree. Discordant imaging may necessitate bilateral neck exploration [8]. The finding of discordant imaging highlights the need for the surgeon to review the imaging prior to the operation. With clinical experience in interpreting these studies, one can gain insight into their degree of reliability. For example, if the sestamibi scan is quite convincing but the ultrasound is equivocal, it would be reasonable to proceed with MIP based on the results of the sestamibi scan, and if an appropriate drop in PTH is obtained, to complete the operation as MIP. Clearly documenting the operative findings (with potential identification of the ipsilateral normal gland) would be extremely helpful if a reoperation is needed in the future. Failure to localize a parathyroid adenoma preoperatively necessitates a bilateral neck exploration that may require a slightly longer incision. Patients with non-localizing preoperative imaging are more likely to have multigland disease, and caution should be taken when a single adenoma is removed after exploration of one side of the neck. IOPTH may be helpful in directing the need to explore the contralateral neck.

2.3.2 Failure of IOPTH to Fall Appropriately

A common scenario that occurs during MIP is successful removal of a parathyroid adenoma but without an appropriate fall in PTH. In this case, it is critical to explore for other enlarged parathyroid glands. One should begin the exploration on the side of the neck where the first enlarged adenoma was removed. If an additional enlarged gland is found, it should similarly be removed. The identification of multigland disease is an indication to proceed with bilateral neck exploration. Bilateral exploration often requires extending the incision and mobilizing both sides of the neck, though bilateral exploration can often be performed through a minimal incision. The gold

standard would be to identify all four parathyroid glands and remove the enlarged gland or glands. It is critical not to remove normal parathyroid glands. If a normal gland is found in this situation, it is helpful to take a small biopsy and confirm its identity by frozen section. The location of the normal gland should be marked with a 4-0 Prolene suture to aid in identification should reexploration be needed in the future. Occasionally a biopsy specimen from a normal-appearing gland is reported to be hypercellular parathyroid tissue. If the gland is of normal size, it is unlikely to be causing the elevation in PTH and should not be removed. The IOPTH can be checked at the end of bilateral neck exploration.

If four parathyroid glands have been identified and the enlarged gland or glands have been removed but the PTH remains elevated, no further exploration should occur during this operation. The finding may be due to laboratory error or an ectopic parathyroid gland, and it would not be in the patient's best interest to proceed in further exploration once four parathyroid glands have been identified and the abnormal glands have been removed. The patient may be better served by drawing an additional PTH level in the recovery room, with further imaging if the hyperparathyroidism persists postoperatively.

2.3.3 Other Methods of MIP

Other refinements of MIP include minimally invasive radioguided parathyroidectomy, video-assisted parathyroidectomy, and endoscopic parathyroidectomy [9–11]. The latter two alternative MIP approaches have not been widely adopted but may be applied in the appropriate clinical situation. MIP will continue to evolve as technological developments allow for improvements in the approach to parathyroidectomy.

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Subtotal Parathyroidectomy for Parathyroid Hyperplasia

3

Göran Åkerström, Per Hellman, and Ola Hessman

3.1 Introduction

Parathyroid adenomas are known to cause 75–85% of cases of primary hyperparathyroidism (pHPT). Parathyroid chief-cell hyperplasia was described in 1958, and has been reported to occur in 15–25% of pHPT patients. Hyperplasia has remained a problem in parathyroid surgery, as results are inferior if multigland involvement is not recognized. Adenomas and hyperplastic glands are often indistinguishable from one another by histopathological examination, and many physicians have preferred to classify hyperplasia as multigland disease (MGD). Nodular hyperplasia is common, and individual nodules often represent monoclonal lesions, which may grow to occupy an entire gland and appear as adenomas. In sporadic pHPT, causes of stimulation often are not identified, in contrast to HPT that is secondary to uremia or long-term lithium therapy. The hyperplasia or MGD in sporadic cases occurs more frequently in patients with mild hypercalcemia, especially in postmenopausal women with vitamin D deficiency, slight renal impairment, or both. It is also common in young patients who have been diagnosed early with renal stone disease [1]. MGD is the common disease entity in familial pHPT, as all parathyroid cells harbor the germline genetic alteration. About 5% or more of pHPT patients have familial HPT related to the multiple endocrine neoplasia (MEN) syndromes, most frequently MEN1 (due to mutations of the *MEN1* gene, encoding the menin protein). In this syndrome, 95% of probands have developed HPT by the age of 45 years, whereas in MEN2A (due to *RET* oncogene mutations), HPT affects only 20–30% of patients. In the recently discovered, very rare MEN4 syndrome (due to *CDKN1B* mutations), both single adenomas and MGD have been reported [2]. Hereditary disease also occurs as familial isolated HPT, including patients with *MEN1* gene mutations, where other endocrinopathies have not been expressed. In the rare HPT-jaw-tumor syndrome (HPT-JT, due to mutation of the *HRPT2/CDC73* parafibromin gene), patients may have single or multiple adenomas, and parathyroid carcinoma occurs in 10–15% of patients. Patients with familial hypocalciuric hypercalcemia (FHH), caused by heterozygous mutation in the calcium sensing receptor (*CASR*) gene, need to be differentiated from those with other syndromes because they generally should not be subjected to parathyroid operations. Homozygous *CASR* gene mutations cause neonatal severe pHPT with marked four-gland hyperplasia, and urgent parathyroidectomy may need to be performed in infancy.

Bilateral cervical exploration under general anesthesia has been the standard procedure for treatment of pHPT, with excellent cure rates and a low incidence of complications when done by experienced endocrine surgeons. During the past decade, improvement of imaging techniques for adenoma localization, using sestamibi scintigraphy (MIBI) with SPECT and neck ultrasound, has led to the increased use of minimally invasive procedures for the removal of parathyroid adenomas [3]. Concordant MIBI and ultrasound localization has been reported in about 60–70% of patients and has been suggested to justify a focused operation, with intraoperative parathyroid hormone (IOPTH) monitoring to verify successful adenoma excision. Both MIBI and ultrasound localization have been less useful in cases of MGD, especially in the presence of multinodular goiter. Even when combined with IOPTH monitoring, these tests sometimes fail to recognize the presence of MGD [4]. It is generally recommended that all patients with suspected MGD or nonconcordant imaging should undergo bilateral neck exploration to detect multigland involvement and safely remove diseased glands.

In MGD of sporadic pHPT, two-gland involvement has been most common (65%), occurring as double adenoma (2–5%) or nodular hyperplasia; both upper parathyroid glands seem to be more often affected. Three-gland involvement has been reported in about 25%, and four-gland involvement has been less common (about 10%). Because

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J.R. Howe (ed.), *Endocrine and Neuroendocrine Surgery*, Springer Surgery Atlas Series, DOI 10.1007/978-3-662-54067-1_3

recurrence rates have been low, many have considered it sufficient to excise only the enlarged glands in patients with sporadic pHPT [1]. The presence of familial HPT, and especially MEN1, is important to recognize because the syndrome has been associated with aggressive HPT with frequent recurrence after surgery. MEN1 patients typically have asymmetric MGD with asynchronous lesions that are easily misinterpreted as single adenomas when normal glands coexist with the enlarged ones. Although removal of a single gland may result in periods of normocalcemia also in MEN1, a higher recurrence rate and earlier recurrence has been reported with anything less than subtotal parathyroidectomy. The operation in MEN1 patients should aim to visualize all four parathyroid glands, to allow removal of the largest glands and leave the least involved gland as a remnant. The primary bilateral operation serves the important goal of identifying and appropriately treating the MGD. A unilateral operation not only may fail to detect the MGD but also risks removing a normal gland that might preferably be selected as the remnant [1, 4]. In addition, early recognition of MEN1 is important, in order to allow treatment of the pancreaticoduodenal and pituitary endocrinopathies and thymic tumors, which may cause severe symptoms and premature death in MEN1. Routine cervical thymectomy has also been claimed to reduce the risk for development of malignant thymic carcinoids.

Figure 3.1

Placement of a collar skin incision 3 cm above the sternal notch is often the preferred position for subtotal parathyroidectomy in an elderly person, as this will leave a scar in the lower neck (*arrow a*). In younger individuals, access may be through a smaller incision (2.5–3 cm), placed slightly higher, at the level of the thyroid isthmus, to avoid keloid formation (*arrow b*)

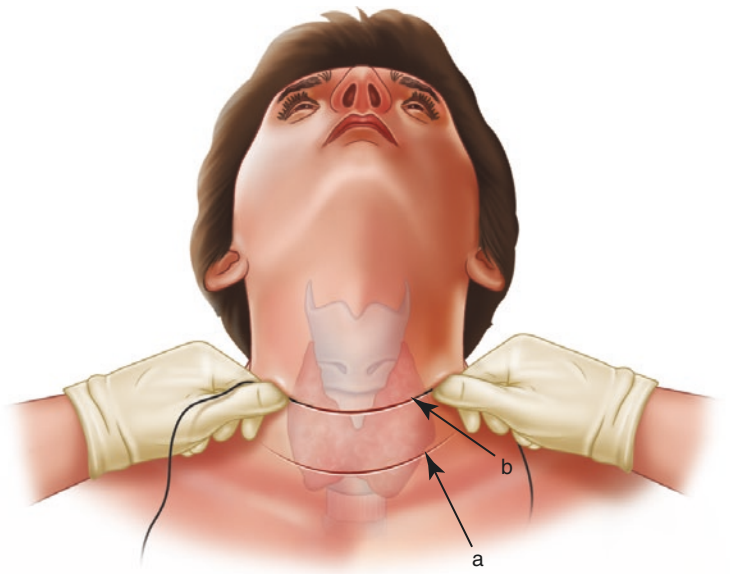
3.2 Techniques of Subtotal Parathyroidectomy

3.2.1 Positioning of the Patient and Skin Incision

To ensure that the incision is symmetric and the scar can be concealed in a skin crease, the surgeon should mark the incision prior to surgery with durable ink while the patient is in an erect position with a nonextended neck. At operation, optimal exposure is obtained with pillow support under the shoulders and a moderately extended neck, which will mobilize the thyroid up from the lower neck. The head should have support by a foam pillow, with the arms tucked along the sides of the body to reduce the risk of incision asymmetry.

The neck is opened by a limited (3–4 cm) collar skin incision 3 cm above the sternal notch, which will leave a scar in the lower neck, the preferred position for an elderly person (Fig. 3.1). In younger individuals, access may be through a smaller incision (2.5–3 cm), placed slightly higher, at the level of the thyroid isthmus, to avoid keloid formation (Fig. 3.1). Subplatysmal skin flaps are dissected with shielded Teflon electrocautery. The superficial fascia and strap muscles are separated in the midline from the sternal notch to the thyroid cartilage incisura (thyroid notch) and pulled laterally by retractors.

Figure 3.1



3.2.2 Normal Parathyroid Anatomy

Autopsy studies have revealed the location of normal parathyroid glands (Fig. 3.2a, b) [1] and have indicated that patients subjected to parathyroid operations should always be considered to have at least four parathyroid glands. Nearly 15% of normal persons harbor supernumerary glands, which may be enlarged in patients with hyperplasia/MGD. Recognizing symmetry in location also can be of help in visualizing pathological glands, as the superior glands have contralateral symmetry in about 80% of cases, and the inferior glands in about 70%. Both pairs of glands can be above or below the junction of the recurrent nerve and inferior thyroid artery, however.

3.2.3 Fascial Layers

The strap muscles and the superficial cervical fascia are dissected from the thyroid surface, and the middle thyroid vein

Figure 3.2

The localization areas of normal superior (**a**) and inferior (**b**) parathyroid glands. (Numbers represent percentages)

Figure 3.3

Visualization of the posterior border of the thyroid lobe, with typical locations of enlarged superior and inferior parathyroid glands

is divided and ligated to allow dissection within the "cotton-wool" plane lateral to the thyroid. In the lower neck, blunt dissection should safely push the thymus, the inferior parathyroid, and the recurrent laryngeal nerve towards the midline. The pretracheal fascia engulfs the thyroid in two layers, which laterally join to form the vascular sheath. The superficial fascial layer is dissected on the thyroid surface and traction is applied for visualization of the posterior border of the thyroid lobe (Fig. 3.3); on the right side, care is taken to avoid injury to a nonrecurrent laryngeal nerve. The fascia is distinct around the superior thyroid lobe but is more friable at the middle and lower thyroid. If the recurrent laryngeal nerve must be exposed, the covering thin fascia is cut longitudinally along the direction of the nerve to open up the posterior space. In children, this fascia layer over the recurrent laryngeal nerve is often distinct.

Figure 3.2

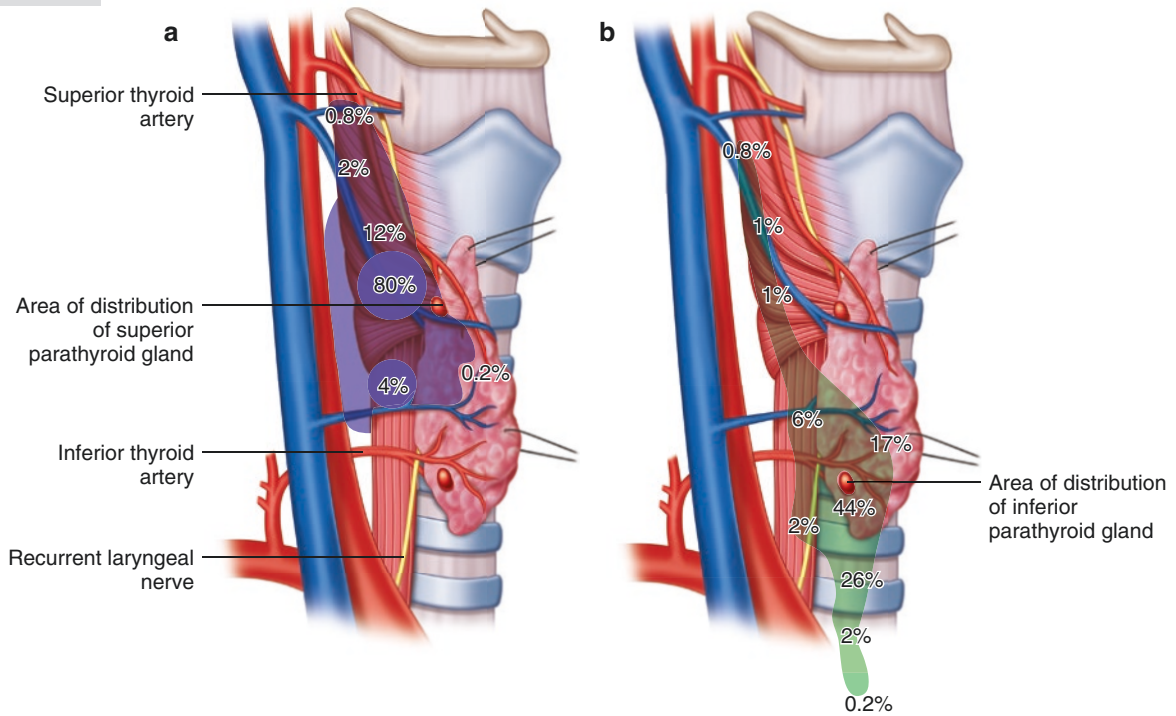
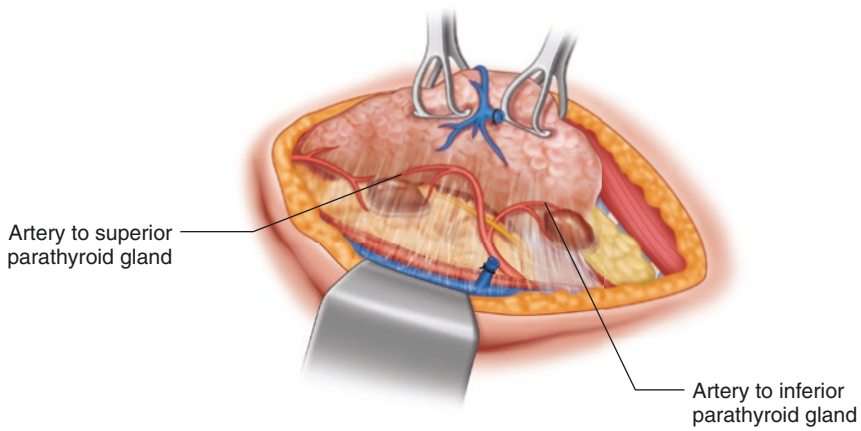


Figure 3.3



3.2.4 Exposure of Parathyroid Glands

When the thyroid lobe has been mobilized, the surgeon should inspect the most common locations of the parathyroids. The strategy of exposure is expressed as "not removing anything before seeing everything." If the thyroid capsule has been exposed appropriately, palpation with an instrument may reveal glands sliding, together with lobules of fat, between the pretracheal fascia layers, from where they will be delivered when the ventral fascia has been transected on the thyroid lobe surface. For superior glands, the most pertinent area extends 1–2 cm around and above the nerve/artery junction; for inferior glands, the area is around the lower thyroid pole and the insertion of the thyrothymic ligament. The localization areas for normal superior and inferior parathyroid glands are depicted in Fig. 3.2, and typical locations of enlarged glands in Fig. 3.3. At operation, the enlarged pathological parathyroid glands can be identified by a brownish-

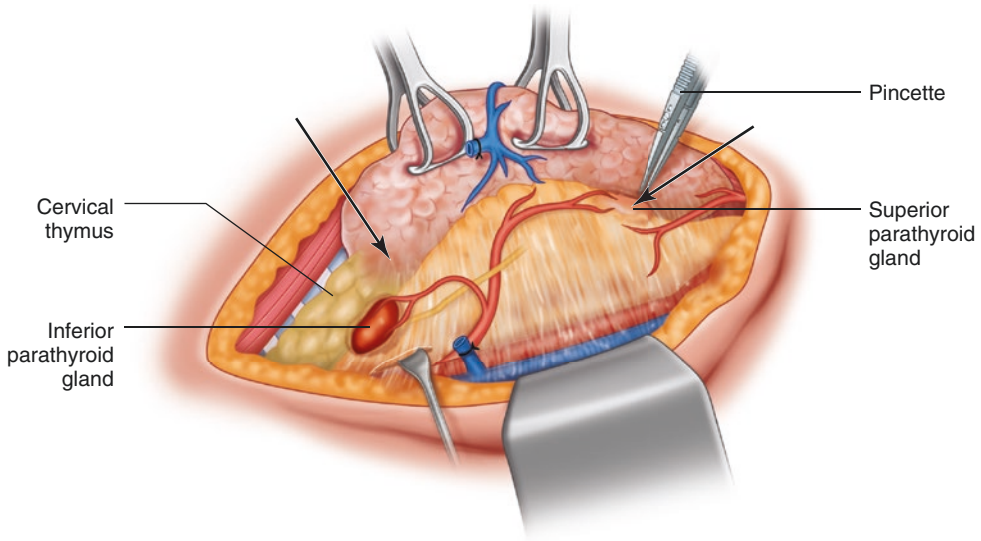
Figure 3.4

The initial phase of the operation is focused also on exposure of normal-sized glands, as this will determine the appropriate strategy of parathyroidectomy. The color of normal glands will generally be yellow or brownish-yellowish; when the color is pale, the texture can help to distinguish a normal parathyroid from a tiny lobule of fat or the thymus

reddish color (Fig. 3.3), glistening homogenous surface (easily separating from surrounding fat), and a palpable but soft consistency. The thyroid will generally appear more reddish, with a firm and nodular texture. Lymph nodes can be variable, either pale or reddish in color, and often lack a well-circumscribed texture; they generally will not separate as easily from surrounding fat.

Interest during this initial phase of the operation is focused also on exposure of normal-sized glands, as this will determine the appropriate strategy of parathyroidectomy. The color of normal glands will generally be yellow or brownish-yellowish; when the color is pale, the texture can help to distinguish a normal parathyroid from a tiny lobule of fat or the thymus (Fig. 3.4). At operation, the search for both pathological and normal parathyroid glands should be systematic.

Figure 3.4



3.2.5 Superior Glands

The superior glands may be hidden in clefts on the thyroid surface, especially if the patient has a nodular goiter (Fig. 3.5), but are rarely deeply intrathyroidal in the superior thyroid lobe. The glands may be situated on or under the tubercle of Zuckerkandl, on or under artery branches or the recurrent laryngeal nerve, or they may be concealed close to (or even within) the ligament of Berry.

Figure 3.5

The superior glands may be hidden in clefts on the thyroid surface, especially if the patient has a nodular goiter but are rarely deeply intrathyroidal in the superior thyroid lobe (*arrow* indicates a superior parathyroid glands partly hidden in the thyroid parenchyma)

Figure 3.6

Superior parathyroid gland with para-esophageal location

The glands can also be para-esophageal or retro-esophageal (Fig. 3.6), retro-pharyngeal, or located towards the tracheo-esophageal groove, but they will then generally be posterior to the recurrent nerve. A pathological gland can often be readily identified by palpation as a circumscribed but soft and movable tumor. The posterior branch of the superior thyroid artery often provides circulation to a superior parathyroid gland by a collateral to the inferior thyroid artery; the collateral can be spared by dissection close to the posterior thyroid border when preserving a normal parathyroid.

Figure 3.5

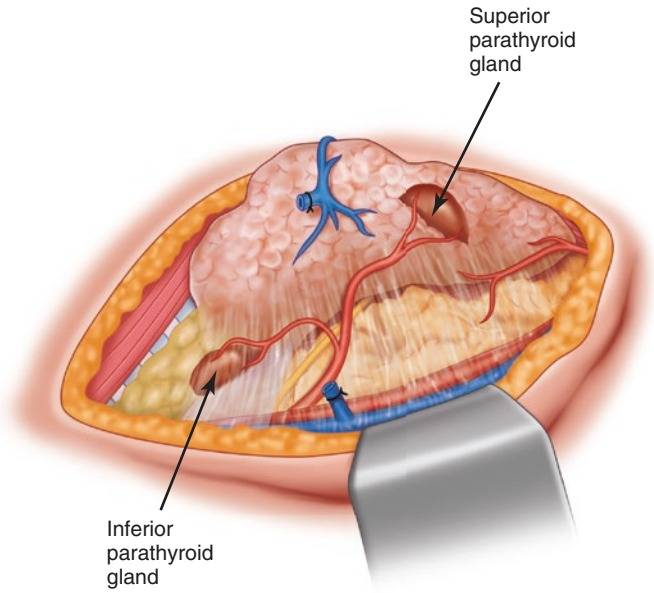
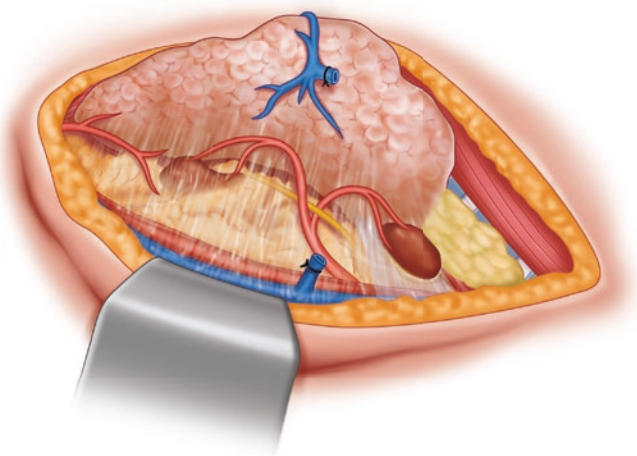


Figure 3.6



The superior glands can sometimes also be on the ventromedial side of the upper thyroid lobe, where they may be concealed by being flat and adherent to the surface of the thyroid capsule (Fig. 3.7). To reveal these glands, the posterior branch of the superior thyroid pedicle may have to be ligated, to allow medial rotation of the upper thyroid pole for exploration of its ventral surface. The posterior branch of the superior thyroid artery often provides collateral circulation to a superior parathyroid gland as described above.

Less than 1% of superior parathyroid glands are undescended, occurring up to 2 cm above the thyroid pole, typically medial to the vascular sheath and the carotid bifurcation. Such glands may be difficult to find, as they may be flattened out towards the pharyngeal wall and may be covered by pharyngeal muscles. A lateral approach between the sternocleidomastoid and strap muscles, anterior to the vascular sheath, can open this area.

As many as 30–40% of enlarged superior glands may be displaced by swallowing maneuvers to ectopic positions,

Figure 3.7

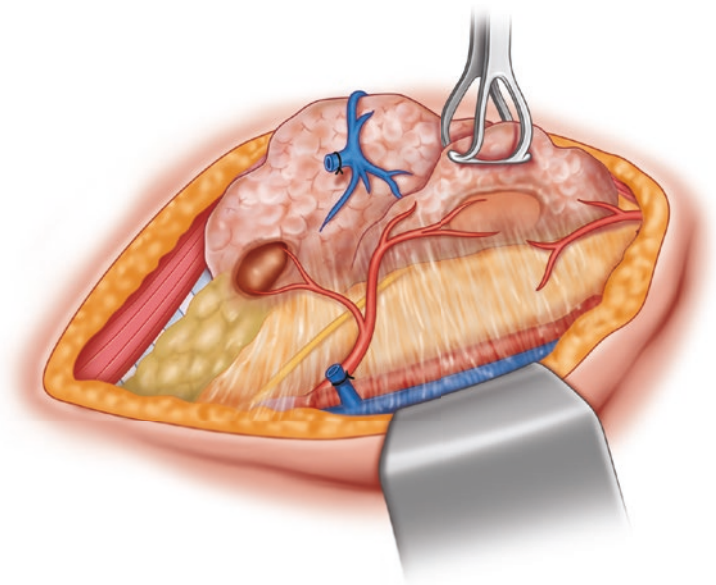
Superior parathyroid gland adherent to the ventromedial surface of the thyroid capsule

by descending caudally in the tracheo-esophageal groove or along the esophagus towards the posterior mediastinum, in a compartment deep to the fascia and posterior to the nerve (Fig. 3.8a). The lower the gland descends towards the mediastinum, the more posterior becomes the location.

A gland may be identified by palpation after dividing the posterior sheath of the pretracheal fascia from the superior thyroid pole to the inferior thyroid artery, and introducing a finger along and behind the esophagus (Fig. 3.8b).

The gland may be pulled by traction along a prominent vascular stalk, turning caudally behind the inferior thyroid artery. These glands can be in the posterior superior mediastinum, and the space may have to be opened by incising the posterior fascia caudal to the inferior thyroid artery, carefully avoiding the recurrent nerve, which will be lateral to the compartment of descent. Occasionally, such glands may be in the midline, covered by a dense fascia, and may then be difficult to remove.

Figure 3.7



MIBI scintigraphy with SPECT can reveal the posterior and caudal displacement of these superior glands. It is crucial to distinguish them from inferior glands, which always have an anterior location in the cervical or mediastinal thymus. Table 3.1 outlines a strategy for locating a displaced superior gland.

3.2.6 Inferior Glands

Owing to their long embryological descent, inferior glands are more variably distributed and often more difficult to find than the superior ones. Enlarged inferior glands seem to be displaced by swallowing less often than enlarged superior

Figure 3.8

(**a**) As many as 30–40% of enlarged superior glands may be displaced by swallowing maneuvers to ectopic positions, by descending caudally, either (**1**) in the tracheo-esophageal groove or (**2**) along the esophagus toward the posterior mediastinum, in a compartment deep to the fascia and posterior to the nerve. (**b**) An enlarged superior parathyroid gland displaced to a posterior compartment deep to the fascia. Running a finger along and behind the esophagus may identify the displaced gland by palpation. (**c**) Displaced glands located by MIBI scintigraphy with SPECT

glands. Like normal glands, around 85% are found around the inferior thyroid pole (*see* Fig. 3.2); about 26% occur in the thyrothymic ligament or within the cervical thymus (see Figs. 3.2, 3.5, 3.6, 3.7 and 3.8b).

Glands on the posterolateral or ventral surface of the lower thyroid pole can often be flattened out within the thyroid capsule, or concealed in clefts of a nodular thyroid, and an artery branch can sometimes be followed to its location. About 1% can be completely intrathyroidal (more often than superior glands); these may be recognized as a palpable nodule in the lower thyroid pole up to the middle of the thyroid. These glands are efficiently visualized by ultrasound, preferably prior to operation. If deeper, they are most often delivered by resection of the lower thyroid pole, or by thyrotomy if opening of the parathyroid capsule can be safely avoided. This technique is preferred to hemithyroidectomy, which may make reoperative surgery more difficult if it later becomes necessary.

Figure 3.8

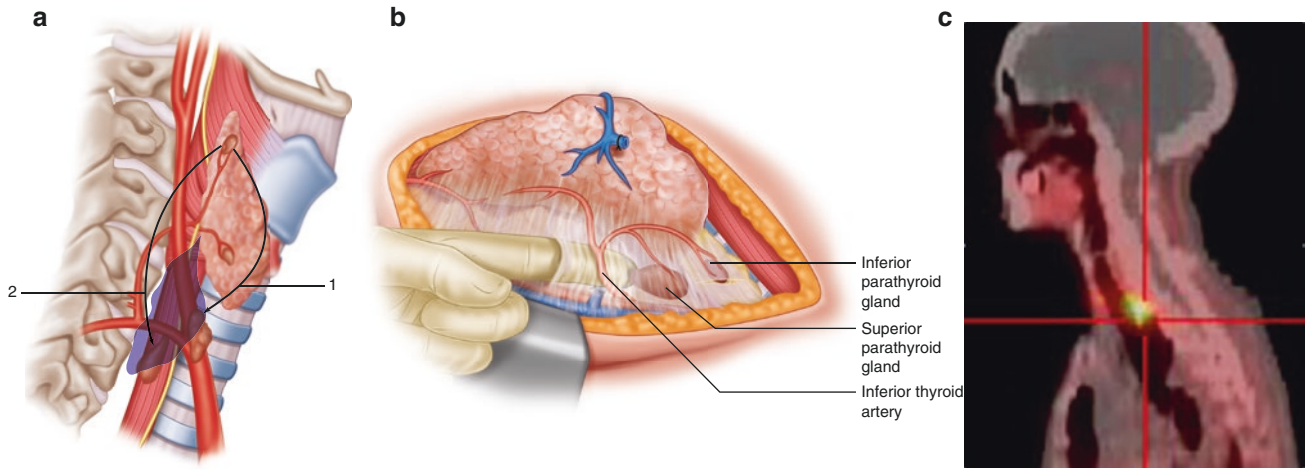


Table 3.1 Strategy for locating a displaced superior parathyroid gland

1. Carefully explore the lateral, posterior, and medial thyroid surfaces and palpate the thyroid lobe to find a rare intrathyroidal parathyroid tumor.
2. Re-explore the juxta-esophageal regions, as far as possible into the posterior mediastinum.
3. Search for an undescended superior gland by exploring the superior thyroid pedicle region.
4. Mobilize the superior pole of the thyroid lobe for dissection of its posteromedial aspects, with ligation of the posterior vascular pedicle if needed.

About 2% of inferior glands can be located close to the trachea, towards the tracheo-esophageal groove but anterior to the recurrent laryngeal nerve (*see* Fig. 3.2). About 8% are more cranially located and can be found around the nerve/artery junction or higher along the line of embryological descent (*see* Fig. 3.2).

The cervical thymus should be dissected free laterally from the surrounding fat (Fig. 3.9), but kept intact to allow inspection on all sides before its fascia is opened over a suspicious lesion. If a gland is not easily found in the cervical thymus, the surgeon should refrain from too much dissection, which may devascularize or remove a normal

Figure 3.9

The cervical thymus should be free-dissected laterally from the surrounding fat but kept intact to allow inspection on all sides before its fascia is opened over a suspicious lesion

Figure 3.10

When inferior glands descend, most move with the thymus toward the anterior mediastinum and fewer glands become located outside the thymus

parathyroid. Instead, other sites should be searched, later dissecting and delivering the thymus into the neck.

About 2% of inferior glands occur in the mediastinal thymus (*see* Fig. 3.2), and an enlarged vessel may sometimes be followed to deliver a tumor (deep mediastinal glands may be supplied from the internal thoracic artery). When inferior glands descend, they move with thymus towards the anterior mediastinum (Fig. 3.10).

Figure 3.9

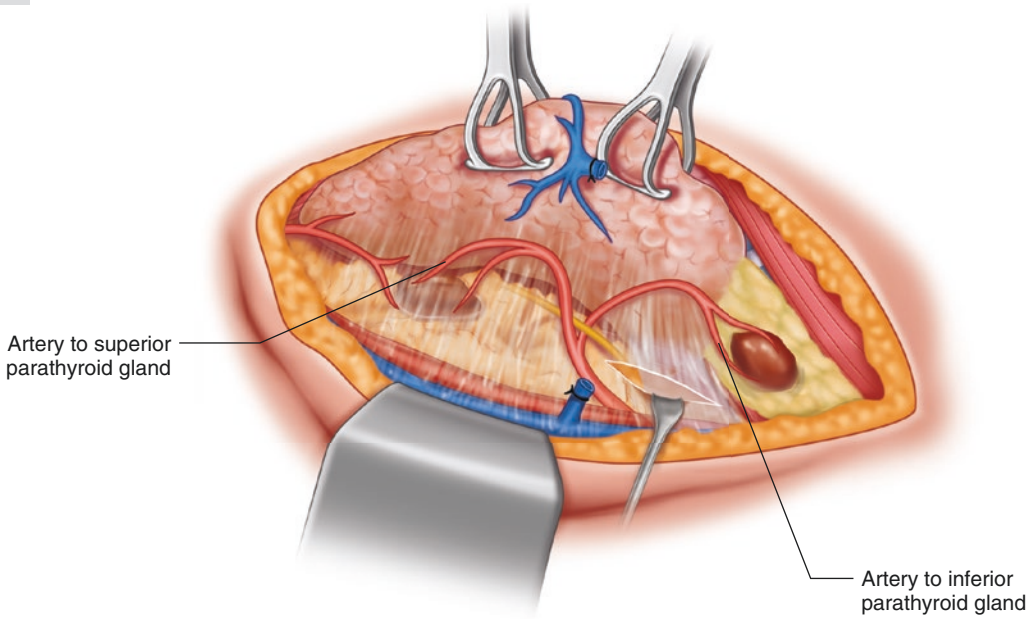
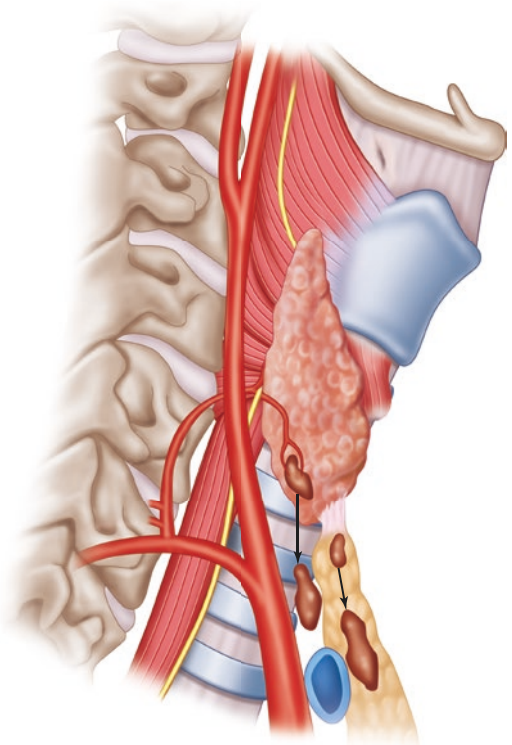


Figure 3.10



Continued traction with repeated forceps grips can deliver a major part of the thymic gland (10–15 cm) and a majority of intrathymic parathyroids from a cervical incision. The dissection downwards is not forced, but instead the thymus is pulled by gentle traction and blunt finger dissection after ligation or clipping of small veins entering the posterior or lateral thymus from the innominate vein (Fig. 3.11a). The delivered thymus is dissected, as glands may be deep in the thymic tissue (Fig. 3.11b).

Figure 3.11

(**a**) Continued traction with repeated forceps grips can deliver a major part of the thymic gland and a majority of intrathymic parathyroids from a cervical incision. The thymus is pulled by gentle traction and blunt finger dissection after ligation or clipping of small veins entering the posterior or lateral thymus from the innominate vein are ligated. (**b**) The delivered thymus has to be dissected as glands may be deep in the thymic tissue

Figure 3.12

Undescended inferior parathyroid glands are found above the thyroid, often together with a rim of thymic tissue; in such cases, the thymus may be typically lacking below the thyroid. The illustration shows an undescended inferior parathyroid attached to a piece of thymic tissue in the vascular sheath. It also shows an undescended superior parathyroid gland located in between the superior thyroid artery branches above the thyroid pole

Undescended inferior glands are rare at primary operations, but occur in 1–3% of reoperative cases (Fig. 3.12a, b). These glands are found above the thyroid, often together with a rim of thymic tissue; in such cases, the thymus may be typically lacking below the thyroid. These glands have a more lateral location than superior undescended glands, closer to the carotid sheath.

Figure 3.11

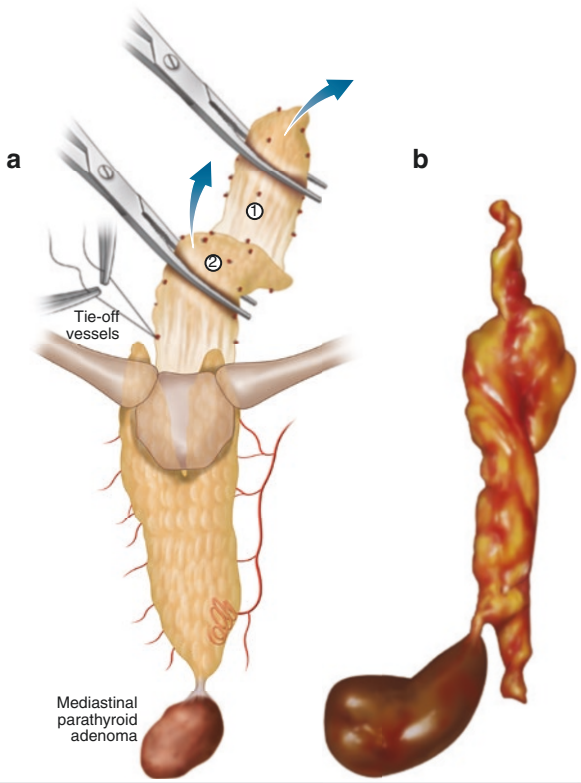
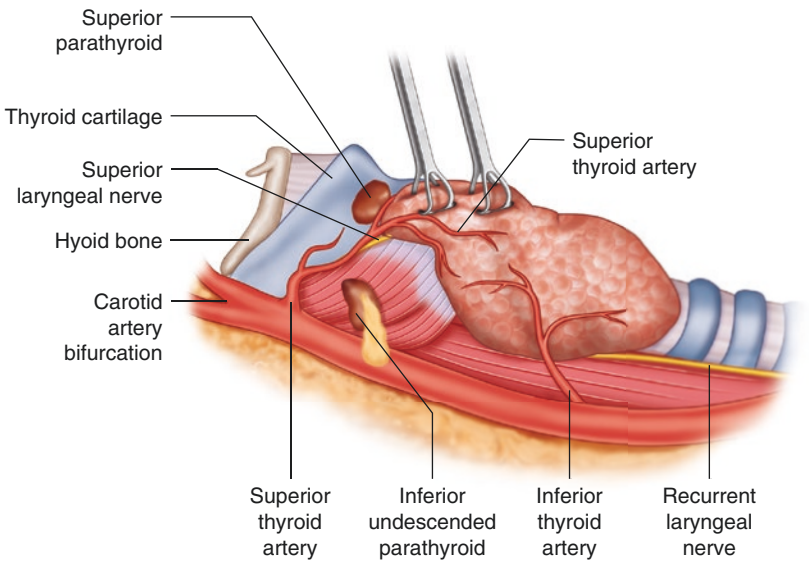


Figure 3.12



Inferior glands may also be "wrongly" descended, appearing in the vascular sheath. In such cases, a cord of fibrous thymus can be seen as a yellow track to the tumor ("yellow brick road"), crossing laterally and upwards from the thyrothymic ligament (Fig. 3.13a, b). MIBI scintigraphy with SPECT can identify these vascular sheath tumors, which can occur from below the carotid artery bifurcation to the level of the clavicle.

Adenomas in the vascular sheath attached to the vagal nerve have been reported but are exceedingly rare. Some have been dissected without nerve injury.

Figure 3.13

"Wrongly" descended inferior glands may be located in the vascular sheath (*left*). A cord of fibrous thymus can be seen as a yellow track to the tumor ("yellow brick road"), crossing laterally from the thyrothymic ligament. This yellow cord can be followed to deliver the tumor (*right*)

Mediastinal adenomas located outside of the thymus (most often ventral to the aortic arch) have been reported in patients with MGD. Rarely, tumors have been found in the aortopulmonary window or other places in the middle mediastinum, or on the left side, lateral to the descending aorta. Many of these are believed to represent superior glands. Mediastinal tumors that cannot be delivered via cervical exploration generally require more extended investigations and preoperative planning. Treatment with thoracoscopy is increasingly being used, and these tumors should not be approached with a primary operation from the neck. Table 3.2 outlines a strategy for locating inferior parathyroid glands.

Figure 3.13

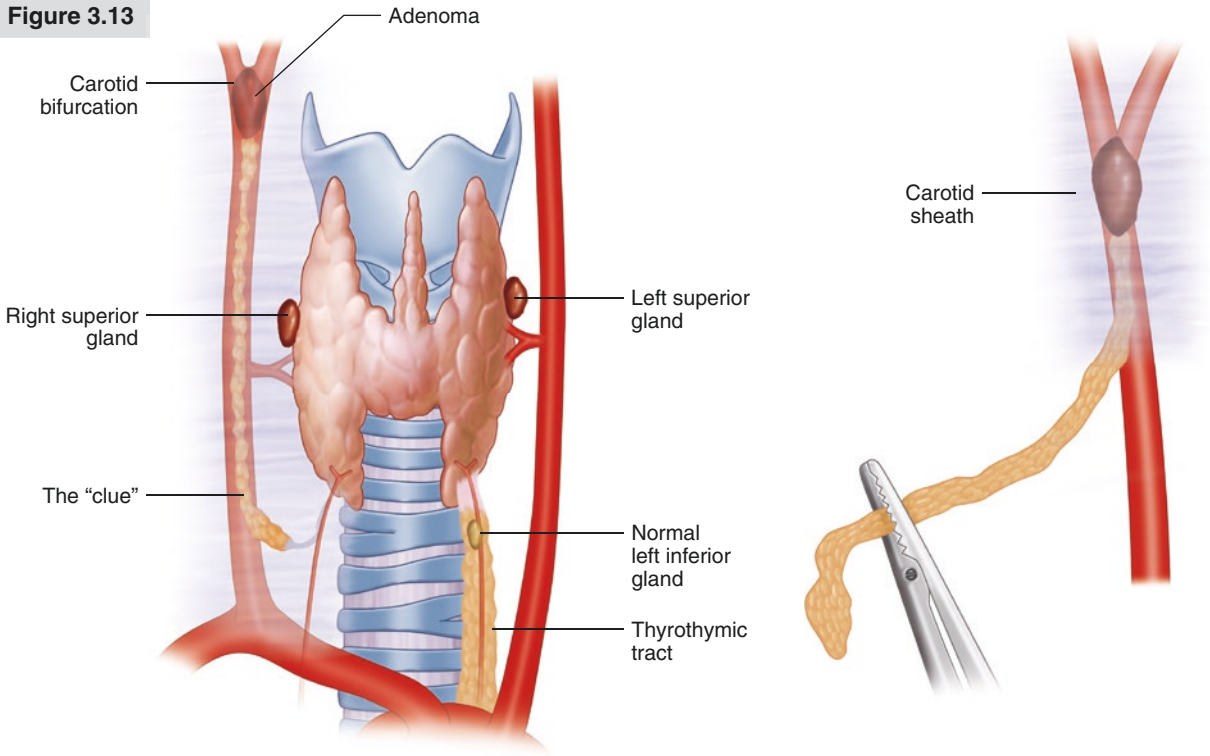


Table 3.2 Strategy for locating a displaced inferior parathyroid gland

1. Carefully palpate the thyroid lobe for an intrathyroidal gland. Consider ultrasound. Most intrathyroidal adenomas are embedded in crevices in the thyroid capsule, and most are easily delivered by incision of the capsule. Those located more deeply require resection of the lower thyroid pole.
2. Remember deficient migration, leaving an undescended inferior gland above the thyroid. Explore medial to and within the carotid sheath from the clavicle to the carotid bifurcation. Is the thymus missing below the thyroid? Is there a track of thymic tissue extending laterally?
3. Extend dissection downwards, dissecting the mediastinal thymus. Space is limited, so bring the thymus up by progressive traction; avoid dividing the thymus before it is delivered.
4. If the inferior gland is not found, it may be low down in the mediastinum. Median sternotomy is rarely performed at the first operation. The gland must be well-localized, then consider left or anterior thoracoscopy, or left thoracotomy.

3.2.7 Supernumerary Glands

Supernumerary glands occur most often as a fifth gland in the thymus, or occasionally between glands in normal locations, where even minute pieces can become enlarged. When performing parathyroidectomy, especially in MEN1 patients and in patients with four-gland involvement, the surgeon should perform routine thymectomy and consider excising fat surrounding glands in normal locations. Divided or multilobated glands must be recognized. If part of a diseased gland is not discovered and removed, the pHPT will persist or recur.

3.2.8 Subtotal Parathyroidectomy: Resection and Verification

Subtotal parathyroidectomy, implying the resection of three or three and one-half glands, is recommended as the first-choice

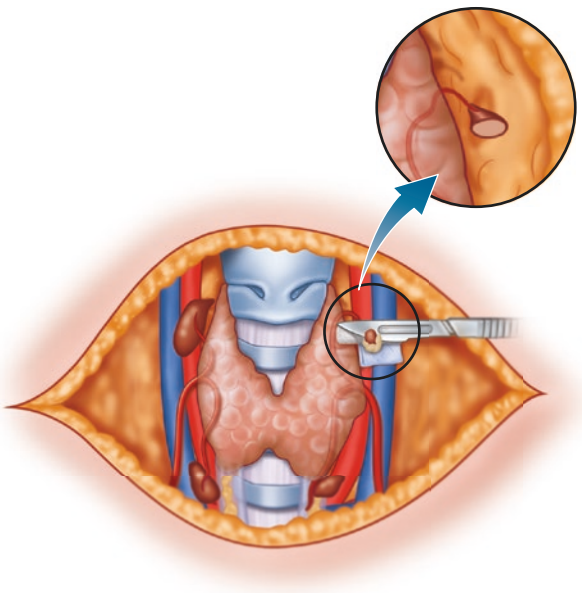
Figure 3.14

Subtotal parathyroidectomy, implying the resection of three or 3.5 glands. The smallest gland is selected as remnant, and is partially resected with a knife, carefully avoiding spillage of parathyroid tissue

operation in patients with parathyroid hyperplasia/MGD, and is preferred if the patient also harbors normal-sized or only moderately enlarged glands (Fig. 3.14). The smallest gland should be selected as the remnant. If the remnant gland is enlarged, it can be partially resected with a knife to a remnant of approximately 40–50 mg, avoiding spillage of parathyroid tissue by cutting against a gauze sponge and with the area closed off by operation cloths. If remnant viability is unquestioned (it bleeds after resection), the other glands can be removed. If the selected remnant has questionable viability, it must be removed and the parathyroid next smallest in size is selected to serve as the remnant. A nonabsorbable suture in the neighboring thyroid marks the site of the remnant.

In our practice, fine-needle aspiration using a syringe filled with 1 mL of saline for rapid PTH determination has generally replaced frozen section analysis for routine verification that an identified or excised specimen is of parathyroid origin.

Figure 3.14



3.3 Results and Conclusions

Unexpected familial disease, which has been reported in 10% of pHPT patients younger than 40 years of age, is a leading cause of failure after minimally invasive or unilateral operations in patients with MGD [1, 2, 4, 5]. It is important to obtain a family history regarding HPT and MEN1-related endocrinopathies in all pHPT patients. Genetic testing and/or biochemical screening is recommended to diagnose MEN1 in all patients found to have multiple gland involvement, or any patient with recurrent or persistent disease after a parathyroid operation [1, 2]. MEN2A-associated pHPT occurs most often with *RET* codon 634 mutations; most patients have mild disease, and it is recommended to excise only enlarged glands. If reoperation after previous thyroidectomy is considered, careful localization of pathological glands is needed. The HPT-JT syndrome requires complex genetic testing for diagnosis; it has been diagnosed in patients with unusually large (or cystic) parathyroid tumors or marked hypercalcemia, and is associated with parathyroid carcinoma in 10–15%. Typical jaw osteofibromas may be present (35%), and the patient may develop renal cysts, adult Wilms tumors, aggressive uterine tumors, and rarely pancreatic carcinoma and Hurthle cell thyroid tumors. FHH may cause hypercalcemia in children (<10 years of age), at a generally younger age than MEN1 patients, who tend to develop rising serum calcium during their second or third decade of life. FHH patients may have slightly raised PTH values (half the patients have raised serum magnesium), and they typically present with low urinary calcium excretion (<100 mg/24 h) and a calcium/creatinine clearance ratio less than 0.01. HPT patients generally have higher calcium excretion (>125 mg per 24 h) and a ratio greater than 0.02, but they may have a lower ratio (<0.01) because of vitamin D deficiency or the use of thiazides or lithium. Family history or samples from relatives can help distinguish the causes, and a FHH1 (*CASR*) gene test is recommended in patients with a ratio between 0.01 and 0.02; this test can diagnose FHH with 70% sensitivity [1, 2, 4, 5]. Large parathyroid tumors were previously often associated with vitamin D deficiency, but now they are also encountered in patients with familial syndromes, such as MEN1 or the HPT-JT syndrome [1, 3, 5]. The appropriate operation must be selected differently depending on the cause of MGD, and subtotal parathyroidectomy is generally recommended to prevent recurrence, especially in MEN1 patients [1, 2].

Bilateral neck exploration for exposure of the parathyroid glands in patients with MGD should remain an important basis for parathyroid surgery training. The operation may not require imaging, and patients with non-localizing imaging tests should not have to wait until scans become positive, but instead should be offered neck exploration. Nevertheless, preoperative imaging with MIBI scintigraphy and surgeon-performed ultrasound can help to identify glands in unusual locations and may reveal concomitant thyroid abnormalities. Ultrasound-guided fine-needle aspiration for PTH determination can also verify that a lesion with doubtful features is indeed a parathyroid gland. The bilateral operation is recommended in patients with familial disease, in sporadic HPT patients when imaging is discordant or indicates multiple sites, when a focused operation fails, or when IOPTH results are equivocal. To minimize the risk of a failed operation, it is also recommended to diagnose and treat vitamin D deficiency in older patients and to routinely exclude FHH by urinary calcium testing. Routine screening for familial syndromes is proposed in patients younger than 40 years [1, 2].

Subtotal parathyroidectomy is the procedure of choice in patients with parathyroid hyperplasia or MGD. Persistent hypoparathyroidism should be carefully avoided by cautious visualization of normal-sized glands and by leaving an appropriate remnant. In patients with MGD and involvement of three or more glands, cervical thymectomy and removal of fat tissue around the thyroid has been recommended to avoid failure. Should recurrence occur, the remnant may be retrieved if appropriately marked; it can then be resected again or a remaining part of it can be autotransplanted.

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Parathyroid Transplantation

4

Samuel A. Wells Jr

4.1 Introduction

Transplantation of the parathyroid glands as autografts or allografts has been attempted in experimental animals and humans since the early 1900s. In occasional cases, there was histological evidence of autograft survival, but until the 1970s, it had not been documented that transplanted parathyroid tissue alone was sufficient to maintain calcium homeostasis in the host [1, 2]. Since then, the technique of parathyroid autotransplantation has been refined and applied in clinical surgery, primarily for two indications.

The first and most common indication occurs during head and neck operations, primarily total thyroidectomy, in which the parathyroid glands are at risk for inadvertent damage or removal. It may be difficult to preserve any viable parathyroid glands if total thyroidectomy is accompanied by dissection of the central nodal compartment. In this setting, the surgeon should have a liberal attitude of grafting all removed parathyroid glands, including those of questionable viability. Transplantation is relatively simple and consists of grafting slivers of normal parathyroid tissue into a nearby muscle, such as the sternocleidomastoid. Serum calcium levels are monitored postoperatively, and supplemental calcium and vitamin D are administered if significant transient hypocalcemia develops. The results of this procedure are excellent: the incidence of graft-dependent hyperparathyroidism is the same as if normal parathyroid glands were left in situ, and the incidence of permanent hypoparathyroidism ranges from 1% to 5% [3, 4].

The second indication concerns patients with parathyroid hyperplasia, whether primary, as in hereditary forms of hyperparathyroidism, or secondary, as in renal osteodystrophy. The goal is to reduce the parathyroid mass while retaining normal parathyroid function. Formerly, the procedure of choice was subtotal parathyroidectomy (SPT) with removal of three and one-half parathyroid glands, the expectation being that the remaining remnant would function sufficiently to maintain serum calcium within the normal range, yet not over-function and cause recurrent hyperparathyroidism. But the incidence of recurrent hyperparathyroidism after subtotal parathyroidectomy for primary parathyroid hyperplasia approaches 70%, and the treatment is re-exploration of the neck, with either subtotal or total resection of the parathyroid remnant [5]. Because of the high incidence of recurrent hyperparathyroidism and the necessity for a repeat neck exploration to reduce further the parathyroid mass, total parathyroidectomy and transplantation of parathyroid tissue (TPTx) to a heterotopic site, such as a forearm muscle, was proposed as an alternative procedure. With this operation, if graft-dependent hyperparathyroidism develops, a portion of the graft can be removed under local anesthesia.

Regardless of the indication, the technique of grafting is the same. Unlike other solid organ transplants, for which arterial and venous anastomoses are established, the parathyroid grafts receive nutrients from tissue fluid until they develop a blood supply from the surrounding muscle bed within a few days.

In patients with parathyroid hyperplasia, the surgeon also should perform a transcervical thymectomy, as 40% are reported to have ectopic parathyroid glands, and 7% have supernumerary parathyroid glands [6]. It is also recommended that serum levels of parathyroid hormone (PTH) be determined immediately following parathyroidectomy, to reduce the likelihood that hyperfunctioning parathyroid tissue is present.

Whether the initial operation is for primary or secondary parathyroid hyperplasia, the initial step is to identify all four parathyroid glands. If fewer than four glands are identified macroscopically and by frozen-section confirmation, parathyroid transplantation should not be performed, as it is unwise to have hyperfunctioning parathyroid tissue at different anatomical sites. An option is to prepare slivers of parathyroid tissue for cryopreservation, so that grafting can be

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J.R. Howe (ed.), *Endocrine and Neuroendocrine Surgery*, Springer Surgery Atlas Series, DOI 10.1007/978-3-662-54067-1_4

performed later if necessary. If properly performed, the transplantation of cryopreserved parathyroid tissue restores the serum calcium to normal in the majority of aparathyroid patients [7].

Should graft-dependent hyperparathyroidism develop following transplantation, it is critical for the patient to be carefully evaluated, including a sestamibi scan to exclude the presence of ectopic or supernumerary parathyroid tissue. If the parathyroid graft alone is the cause of recurrent hyperparathyroidism, approximately 50% of the grafted tissue should be removed, the amount depending on the degree of hypertrophy in the individual implanted pieces.

4.2 Surgical Technique

As a first step, every attempt should be made to identify all four parathyroid glands. In patients having head and neck procedures, resected parathyroid glands or those of questionable viability are removed, cleansed of fat and adventitia, and placed in a saline bath over plastic-covered ice. In patients with parathyroid hyperplasia, all four parathyroid glands, as well as any supernumerary glands, are removed and placed in iced saline. If possible, the smallest parathyroid gland (without nodularity in the case of parathyroid hyperplasia) should be selected for grafting. The implanted slivers should be no larger than 1 × 3 mm, so that the cells in the center of the piece, as well as those on the edges, will receive adequate nutrition. The parathyroid gland is grasped along its long axis (shown here with DeBakey forceps) and using a scalpel with a #10 Bard Parker blade, whole tissue discs approximately 3 mm thick are sliced and removed (Fig. 4.1). Strips of parathyroid tissue measuring 3 mm are then sectioned from a tissue disc and placed on a flat metal surface, where slivers of parathyroid tissue 1 × 3 mm in size are cut from the strip with a rocking motion of the blade. The slivers are then placed in an iced saline bath awaiting implantation. The parathyroid tissue should be

Figure 4.1

The parathyroid gland is grasped along its long axis (shown here with DeBakey forceps) and, using a scalpel with a #10 Bard Parker blade, whole tissue discs approximately 3 mm thick are sliced and removed. Strips of parathyroid tissue measuring 3 mm are then sectioned from a tissue disc and placed on a flat metal surface, where slivers of parathyroid tissue 1 × 3 mm in size are cut from the strip with a rocking motion of the blade

grafted within 3 h of removal. Attention to detail is critical in this procedure; the incidence of postoperative hypoparathyroidism is minimal if the technique is performed properly.

The hand is placed in a prone position and taped to an armboard; then the forearm is prepared sterilely from above the elbow to the wrist. An area of 5 × 8 cm over the brachioradialis muscle is draped and covered with adhesive plastic. Through a 3- to 4-cm skin incision, the brachioradialis muscle bed is exposed, and a retractor is placed so that both hands are free for grafting the parathyroid tissue (Fig. 4.2). The graft bed need be no larger than 3 × 3 cm.

Using microsurgical instruments, an incision is made in the overlying thin layer of fascia and the muscle fibers are separated (Fig. 4.3). A single parathyroid sliver is placed in each of 15–20 muscle pockets. Alternatively, 5–10 slivers may be placed into each of six pockets, if there is ample room for each sliver within the pocket. It is important that the transplanted parathyroid sliver be buried 2–3 mm below the muscle surface and completely covered by muscle fibers. The muscle is then closed over the parathyroid piece with a single nonabsorbable suture. The ends of each of these marking sutures should be about 2–4 mm in length to help identify the graft site in case graft-dependent hyperparathyroidism develops later and some of the implanted parathyroid tissue must be removed.

The wound is then closed in a standard fashion. Parathyroid graft function can be assessed in the future by determining the serum calcium concentration and by comparing PTH levels in antecubital venous blood from the grafted arm and the nongrafted arm. Figure 4.4 shows a parathyroid sliver in a muscle bed 1 year after grafting.

If parathyroid autotransplantation is being performed with normal glands (such as those devascularized during thyroid surgery), the same procedure is used except the sternocleidomastoid muscle is chosen rather than the brachioradialis.

Figure 4.1

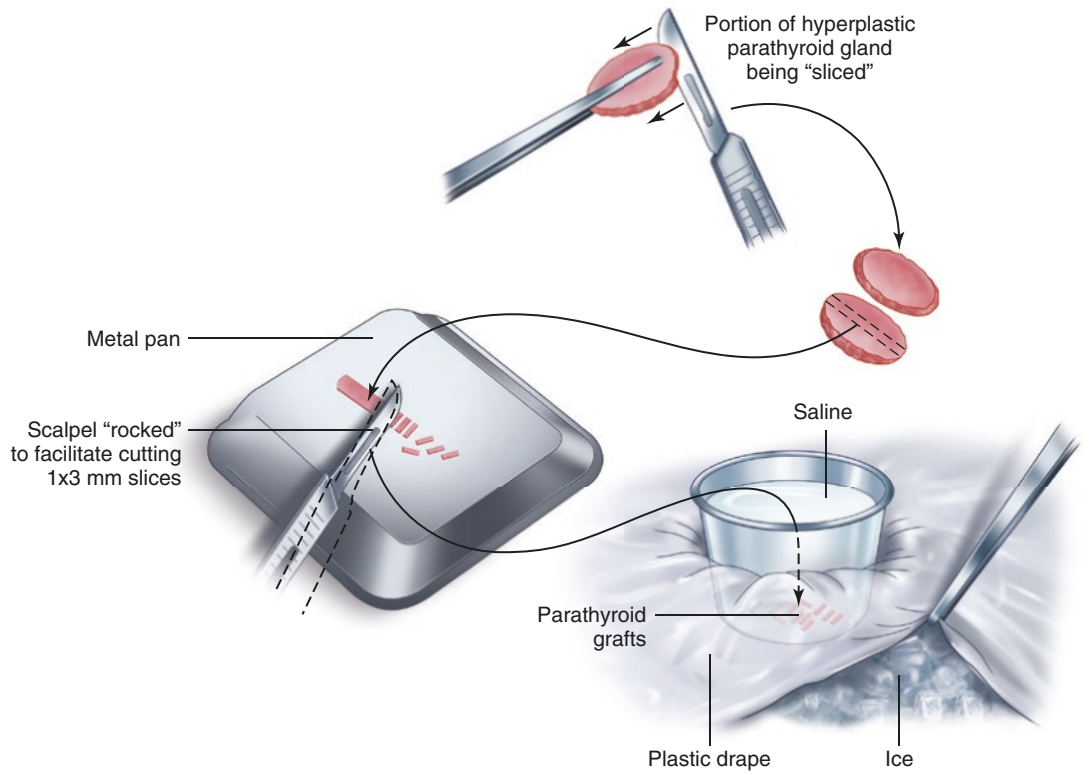


Figure 4.2

In preparation for grafting, the brachioradialis muscle bed is exposed, and a retractor is placed

Figure 4.2

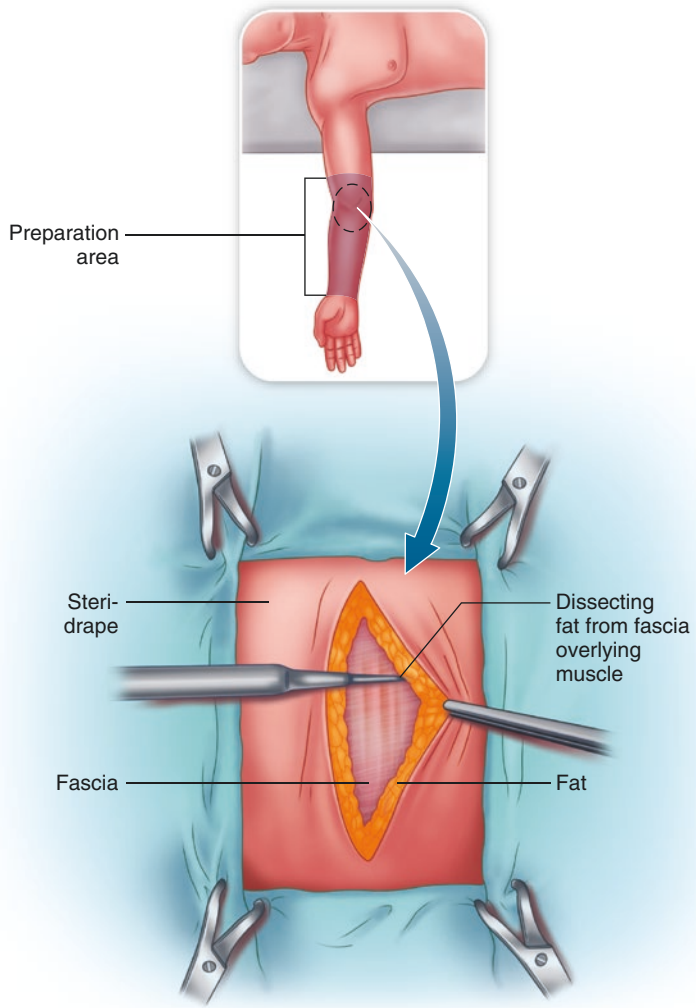

Preparation area
Steri-drape
Dissecting fat from fascia overlying muscle
Fascia
Fat

Figure 4.3

(**a**) An incision is made in the overlying thin layer of fascia and the muscle fibers are separated. (**b**) A single parathyroid sliver is placed in each of 15–20 muscle pockets. (**c**) The muscle is then closed over the parathyroid piece with a single, nonabsorbable suture. (**d**) The transplanted parathyroid sliver must be buried 2–3 mm below the muscle surface and completely covered by muscle fibers. (**e**) The ends of each marking suture should be about 2–3 mm in length

Figure 4.4

Parathyroid sliver in a muscle bed 1 year after grafting (hematoxylin and eosin, original magnification ×100)

Figure 4.3

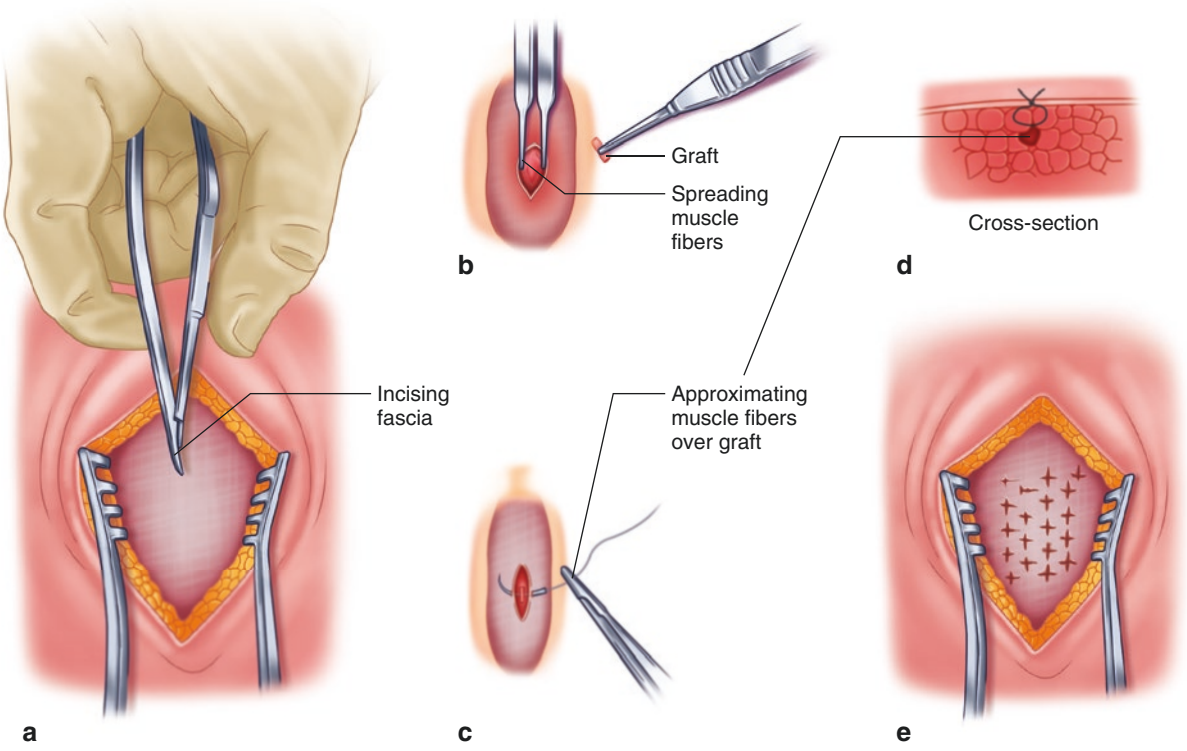
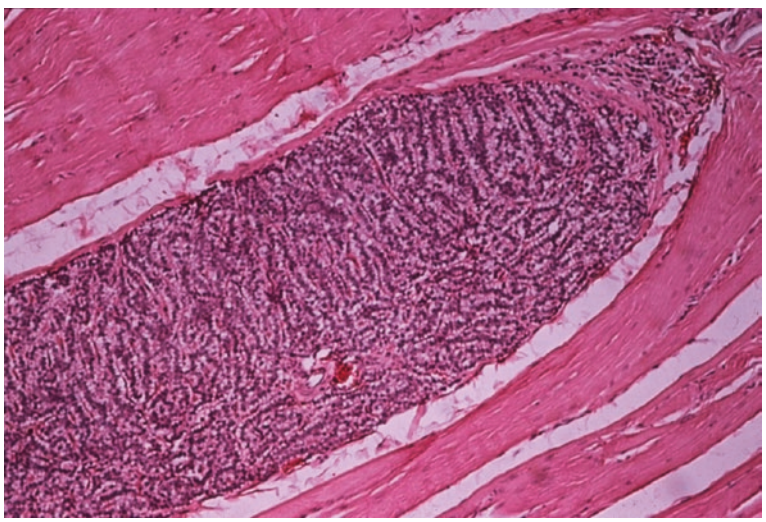


Figure 4.4



4.3 Results and Conclusions

Because parathyroid glands may be compromised during radical head and neck procedures, the transplantation of normal parathyroid tissue at the time of such procedures will substantially reduce the incidence of permanent hypoparathyroidism, and there has been little controversy about this indication. Since the original reports of TPTx in patients with primary or secondary parathyroid hyperplasia, investigators at numerous centers have published their experience with this technique. Results have varied from center to center, but generally they have been comparable to those achieved with SPT. The only randomized controlled trial comparing SPT versus TPTx was a single-institution study in patients with renal osteodystrophy. In this study, patients treated by TPTx had a more rapid normalization of serum calcium and alkaline phosphatase than those treated with SPT, as well as more rapid improvement in radiological signs and greater relief of symptoms such as pruritus and muscle weakness [8]. Unfortunately, no prospective, multicenter, randomized clinical trials have compared the results of the two operative procedures in patients with either primary or secondary parathyroid hyperplasia.

The development of graft-dependent hyperparathyroidism is rare when normal tissue is transplanted, but graft-dependent hyperparathyroidism is relatively common in patients treated with SPT or TPTx for primary or secondary parathyroid hyperplasia. The management of recurrent hyperparathyroidism in patients with parathyroid hyperplasia can be challenging, as repeat neck operations following SPT may be difficult because of substantial scarring. The surgeon also may find it difficult to determine how much hyperfunctioning parathyroid tissue to remove. Conversely, in recurrent hyperparathyroidism following TPTx, the parathyroid grafts can become markedly enlarged and infiltrate the surrounding muscle tissue, making complete removal difficult. It has been recommended that patients with renal osteodystrophy who are not expected to undergo renal transplantation should be managed by total parathyroidectomy without transplantation. The hypoparathyroidism that invariably follows this procedure is a particular concern, however, as it may be associated with a significant further decrease in renal function. Also, the incidence of postoperative hypoparathyroidism has been reported to be higher following TPTx than following either SPT or removal of only three parathyroid glands, which has led some clinicians to favor the removal of only three glands. The predictable short-term (4–8 weeks) hypocalcemia after TPTx can be effectively managed with calcium and vitamin D replacement, typically 2–3 g of calcium carbonate four times daily and 0.25 μg of calcitriol twice daily for 4 weeks, with gradual weaning over the following 4 weeks.

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Mediastinal/Thoracoscopic Parathyroidectomy

5

Richard A. Prinz, John A. Howington, and Catherine A. Madorin

5.1 Introduction

Ectopic parathyroid glands may account for up to 20% of hyperactive glands in primary hyperparathyroidism [1–3]. Ectopic glands most commonly may be found in or near the thymus within the superior mediastinum, but they also may be located within the carotid sheath, posterior to the esophagus, within the thyroid itself, above the hyoid cartilage, or deeper within the mediastinum. Mediastinal glands usually are located in the anterior superior mediastinum, often within the thymus. Almost all of them can be reached through a cervical incision, but about 2% of all mediastinal glands cannot be reached through a cervical approach [3, 4].

The inferior parathyroid glands and the thymus arise from the third pharyngeal pouch. Normally, the inferior parathyroid glands separate from the thymus and remain near the inferior pole of the thyroid. Occasionally, they may migrate into the mediastinum along with the thymus. Because most of these glands will be within or near the thymus, they usually can be resected with transcervical thymectomy [5]. However, not all ectopic mediastinal parathyroid glands are located in the anterior mediastinum. Clark [6] reviewed 64 mediastinal parathyroid tumors and found that 52 (81%) resided in the anterior mediastinum and 12 (19%) in the posterior mediastinum. Russell et al. [7] reviewed 2015 patients operated on for primary hyperparathyroidism and found 15 patients with hyperfunctioning supernumerary glands. Of the 15 glands, 5 were located in the neck, but 10 were found in the anterior mediastinum.

For the 2% of patients with ectopic mediastinal glands that require a thoracic approach, multiple options have been utilized. These include full or partial median sternotomy, anterior mediastinotomy (Chamberlain procedure), closed mediastinal exploration, posterolateral thoracotomy, video-assisted thoracoscopic surgery (VATS), and angiographic ablation [8–16]. Median sternotomy, anterior mediastinotomy, closed mediastinal exploration, and VATS may all be used for anteriorly located glands. Posterior mediastinal tumors are best approached with either thoracoscopy/VATS or a posterolateral thoracotomy [10].

5.2 Preoperative Workup and Imaging

Most patients with ectopic mediastinal glands have previously undergone a negative neck exploration [1, 17]. Patients with suspected mediastinal glands ideally should have at least two concordant imaging studies. Our preference is to perform sestamibi scintigraphy for identification and a chest CT scan for exact localization (Figs. 5.1 and 5.2). If one of these studies is negative, then an MRI is recommended. Selective venous sampling for parathyroid hormone (PTH) levels may even be needed as the second test confirming the intrathoracic location. In a series of 10 patients reported by Ravipati et al. [13], 8 of 9 had positive preoperative localization by sestamibi with concordant CT scans. In one patient with negative sestamibi scintigraphy, the gland was localized by MRI. Nilubol et al. [18] reviewed 32 patients with mediastinal parathyroids and found that sestamibi scintigraphy was correctly positive in 24 of 28 patients (86%)

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J.R. Howe (ed.), *Endocrine and Neuroendocrine Surgery*, Springer Surgery Atlas Series, DOI 10.1007/978-3-662-54067-1_5

and CT scans were correctly positive in 6 of 7 patients (86%). In a study of 13 patients from France, only eight patients had positive concordant imaging; five did not have positive localization of a parathyroid adenoma [19]. Thoracoscopic exploration did not locate the aberrant gland in three (40%) of these five patients. Of the three failures, one patient had a weakly positive sestamibi scan but no lesion was identified on CT scan; the second patient had a negative sestamibi scan with a retrosternal mass seen on CT scan and positive venous sampling; the third patient had a

Figure 5.1

Sestamibi scan showing persistent uptake of the radionuclide by an intrathoracic parathyroid adenoma (*arrow*)

Figure 5.2

CT scan confirming the presence of a parathyroid adenoma in the mediastinum (*arrow*)

negative sestamibi scan with a CT scan and venous sampling suggestive of a mass near the right atrium. All three patients had previous neck explorations [19]. Median sternotomy without adequate preoperative localization has been associated with a failure to find abnormal glands in up to 30% of cases [1]. Thoracic exploration with unclear preoperative imaging is not recommended, especially as the imaging capability of current CT and MRI machines has improved substantially from what was used in many of these studies.

Figure 5.1

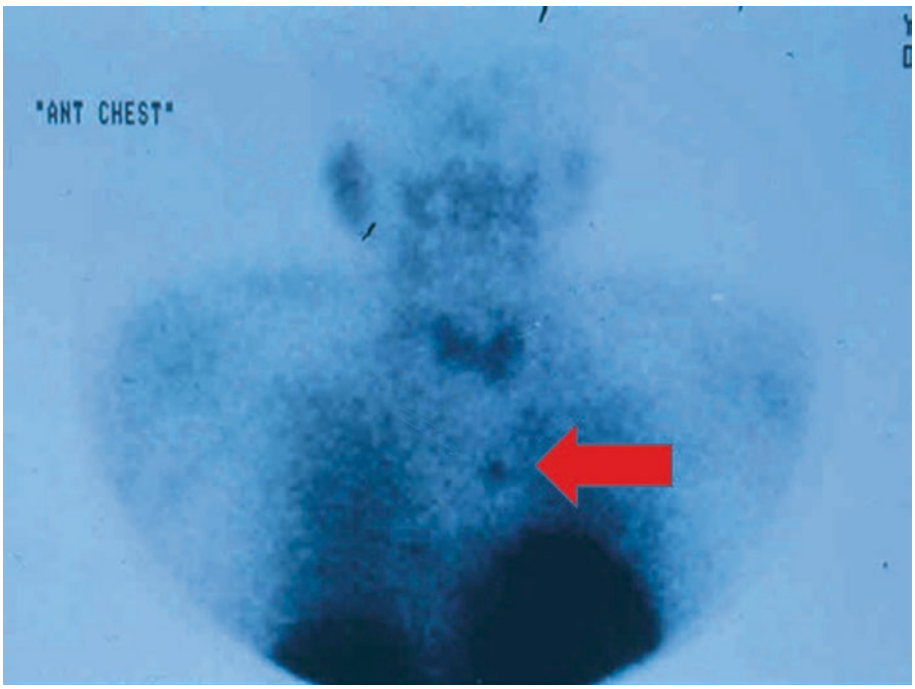
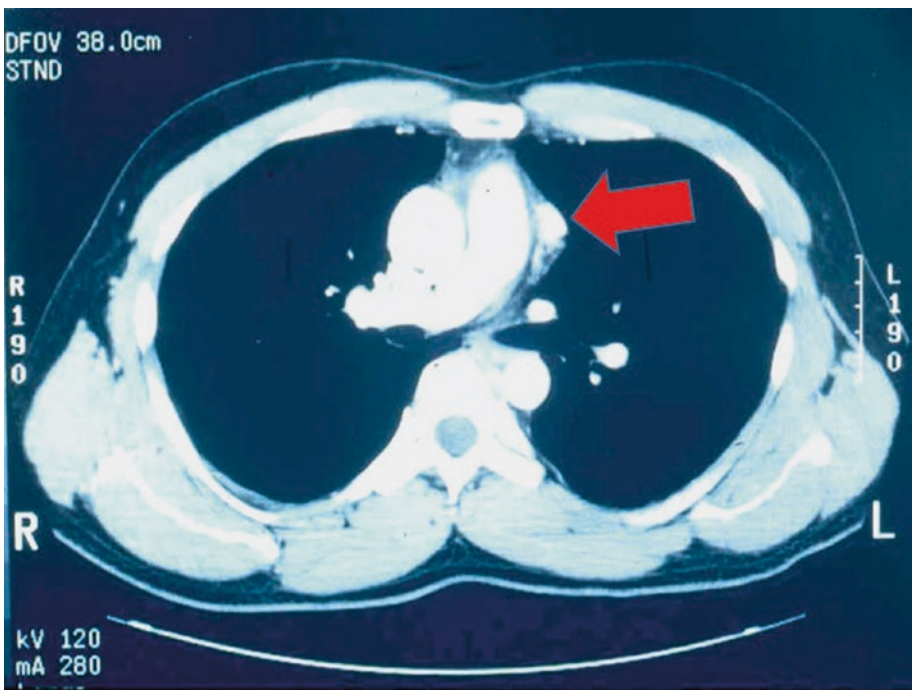


Figure 5.2



5.3 Intraoperative Localization and PTH Monitoring

The intraoperative use of a gamma probe may aid in localizing the parathyroid adenoma within the mediastinum. Abnormal parathyroid tissue takes up ^{99m}Tc-sestamibi more intensely and has a more delayed washout than surrounding tissue, enabling the use of the gamma probe for localization. Ex vivo radioactivity counts of greater than 20% of background may be used to confirm the presence of parathyroid tissue in the specimen [19]. Use of the gamma probe may reduce unnecessary dissection and shorten operating times [20].

Intraoperative PTH monitoring is recommended for all operations for primary hyperparathyroidism, regardless of the approach. We use the criteria for a curative resection of at least a 50% drop and a return to a normal PTH level at 5, 10, or 15 min after resection. If the PTH fails to drop, and frozen section pathologic examination of the specimen confirms the presence of parathyroid tissue, then additional hyperplastic glands must be sought in the neck or the mediastinum. In a retrospective study of 33 patients undergoing mediastinal parathyroidectomy, 7 patients (21%) presented with multiglandular disease that was only discovered because of intraoperative PTH monitoring [21].

5.4 Mediastinal Anatomy

The boundaries of the mediastinum are the parietal pleura laterally, the thoracic inlet superiorly, the superior surface of the diaphragm inferiorly, the sternum anteriorly, and the anterior longitudinal spinal ligaments posteriorly. The anterior mediastinal compartment is bounded posteriorly by a plane along the anterior surface of the great vessels and the pericardium. The contents of the anterior mediastinal compartment include the thymus, anterior mediastinal lymph nodes, fat, and on occasion a retrosternal thyroid or ectopic parathyroid gland. The middle (visceral) compartment contains the trachea, proximal main stem bronchi, esophagus, pericardium, heart and great vessels, lymph nodes, thoracic duct, and the phrenic, vagus, and sympathetic nerves. The posterior compartment shares the same lateral, superior, and inferior boundaries as the anterior compartment. It begins at the vertebral bodies and extends to the transverse vertebral processes. The posterior compartment contains the peripheral intercostal nerves and sympathetic and parasympathetic ganglia.

5.5 Parathyroidectomy Using Video-Assisted Thoracoscopic Surgery (VATS)

Thoracoscopy is performed with the patient under general anesthesia, using a double-lumen endotracheal tube. Arterial lines are only placed selectively. A Foley catheter may be inserted to monitor urine output, as procedures will vary in length and may take longer than anticipated. Baseline circulating PTH levels should be drawn prior to incision.

The lateral decubitus position offers the best exposure for middle and posterior mediastinal ectopic glands (Fig. 5.3). Either a left or right approach may be used for mediastinal parathyroidectomy, depending on the exact location of the aberrant gland. For ectopic glands located in the anterior or anterior superior mediastinum, a modified lateral decubitus position with an angle 45 to 60 degrees from the supine will assist with exposure by allowing gravity to drop the collapsed lung away from the anterior mediastinum. Alternatively, the patient may be left supine with a rolled blanket beneath the back on the operative side, as done for thoracoscopic thymectomy (Fig. 5.4). Port placement and instrumentation will vary from patient to patient, based on the location of the aberrant gland. For ectopic glands in the middle and posterior mediastinum, a 5-mm port is placed in the 5th or 6th intercostal space posteriorly, after infiltration with 0.5% bupivacaine with epinephrine. A 5-mm, 30° scope is placed through the 5-mm port site and the pleural space is explored for any adhesions, effusion, or other abnormality. Next, a thoracic port is placed between the midaxillary and posterior axillary lines, between the 7th and 8th intercostal spaces, based on visualizing the best location for optimal viewing of the planned operative site with the camera. Prior to insertion of the port, an intercostal block with 2–3 mL of 0.5% bupivacaine with epinephrine is performed beneath the insertion site. A 12-mm thoracic port is inserted, and a 10-mm thoracoscope is placed though it. Both 0° and 30° thoracoscopes are acceptable and provide good visualization (we most often use a 30° scope). Next, a 12-mm thoracic port is placed in the 4th or 5th intercostal space in the anterior axillary line after an intercostal

block has been administered with 2–3 mL of 0.5% bupivacaine with epinephrine. This triangulated approach with the camera most inferior and between the other two port sites provides excellent visualization of the middle and posterior mediastinum and reduces "sword-fighting" between the instrument sites and the camera.

For ectopic glands in the anterior or anterior superior mediastinum, the first port is typically placed in the 5th intercostal space in the midaxillary line after infiltration with 0.5% bupivacaine with epinephrine. A 12-mm thoracic port is inserted and a 10-mm thoracoscope is placed though it. Both 0° and 30° thoracoscopes are acceptable and provide good visualization; we most often use a 30° scope. For lesions best approached through the left chest, the ports are placed in the left chest. Likewise, for lesions best approached through the right chest, the ports are placed in the right chest. The lung on the operative side is isolated by the anesthesia service, allowing the lung to deflate. We utilize CO_2 insufflation at a pressure of 6 to 8 mm Hg to assist in exposure and collapse of the lung. If necessary, the lung is retracted away from the operative field. Additional ports should be added after visual exploration of the chest; their optimal location is determined on a procedure-by-procedure basis. Depending on the location of the lesion, the thoracoscope and all other ports should be placed within a 180° arc, which will reduce mirror imaging and instrument overlap. For anterior masses, the ports are placed more anteriorly. The second port (5 mm) is placed at the anterior axillary line in the 2nd or 3rd intercostal space. The third port (12 mm) is placed in the 7th or 8th intercostal space in the anterior axillary line. Three ports (one 5 mm and two 12 mm) are sufficient for nearly all patients.

The gland should be sought in the location determined by preoperative imaging. For glands located in the anterior superior mediastinum, the mediastinal pleura behind the sternum is incised medial to the internal thoracic artery and vein (Fig. 5.5). This incision can be extended superiorly (to the level where the internal thoracic vein turns posteriorly to join the innominate vein on either the right or left side) and inferiorly (down to the diaphragm). This dissection will allow the mediastinum to fall away from the sternum, providing additional working space (Fig. 5.6). Next, the mediastinal pleura adjacent to the pericardium is incised to allow mobilization of the anterior mediastinal fat and thymus. Both visual examination and use of the gamma probe can be used to locate the gland (Fig. 5.7). Long probes can be placed through the inferior 12-mm port to assist in localization of smaller glands. The area of dissection should be based on the preoperative localization. In other words, this procedure is not an exploration but a targeted resection. Dissection can be performed bluntly and/or with hemostatic devices such as a protected-tip cautery, harmonic scalpel, or LigaSure™ (Covidien, Dublin). Larger glands are often visible and are removed with a 2-cm rim of surrounding mediastinal fat, if they are located in the anterior mediastinum (Fig. 5.8). If the glands are not readily visible, all anterior mediastinal fat from the level of the innominate vein down to the diaphragm is removed, and the search for the gland can occur on a back table. Ectopic glands in the middle or posterior mediastinum are typically directly visible and are dissected out with the technique used for complete lymph node dissection. Care should be taken to avoid rupture of the parathyroid capsule, which can lead to seeding and recurrent hyperparathyroidism or parathyromatosis. The vascular pedicle of the gland may be ligated and divided with clips, but most often it is readily controlled with a hemostatic device. The specimen should be placed in a plastic retrieval bag and withdrawn through the most inferior port, as this is usually the widest intercostal space. A chest tube is placed to the apex of the pleural space through the most inferior port site. This tube can be removed 24 h later or when clinically indicated. The two 12-mm port sites are closed in three layers with absorbable sutures. We use a 2-0 Vicryl costal suture, a 3-0 Vicryl subcutaneous suture, and a 4-0 Monocryl subcuticular stitch, and then we seal the sites with glue. The 5-mm port site is closed with a 3-0 Vicryl subcutaneous layer and a 4-0 Monocryl subcuticular suture and is sealed with glue.

Several structures encountered with this approach should be preserved. The phrenic nerve courses along the superior vena cava on the right and anterior to the aortopulmonary window on the left. The recurrent laryngeal nerve is at risk of injury with this procedure, especially on the left within the aortopulmonary window. The left recurrent laryngeal nerve comes off the left vagus nerve, which runs along the left subclavian artery and at the aortic arch passes around the ligamentum arteriosum and continues posteriorly under the aortic arch. On the right, it may be injured with dissection too close to the innominate artery at its origin. With dissection posteriorly, the thoracic duct may be injured, leading to the need for additional procedures and ligation of the duct.

Figure 5.3

The patient is placed in a lateral decubitus position with a gel roll placed in the axilla. (**a**) Shows the right lateral decubitus position; (**b**) shows the left lateral decubitus position. The *inked lines* show portions of the first two port sites

Figure 5.3

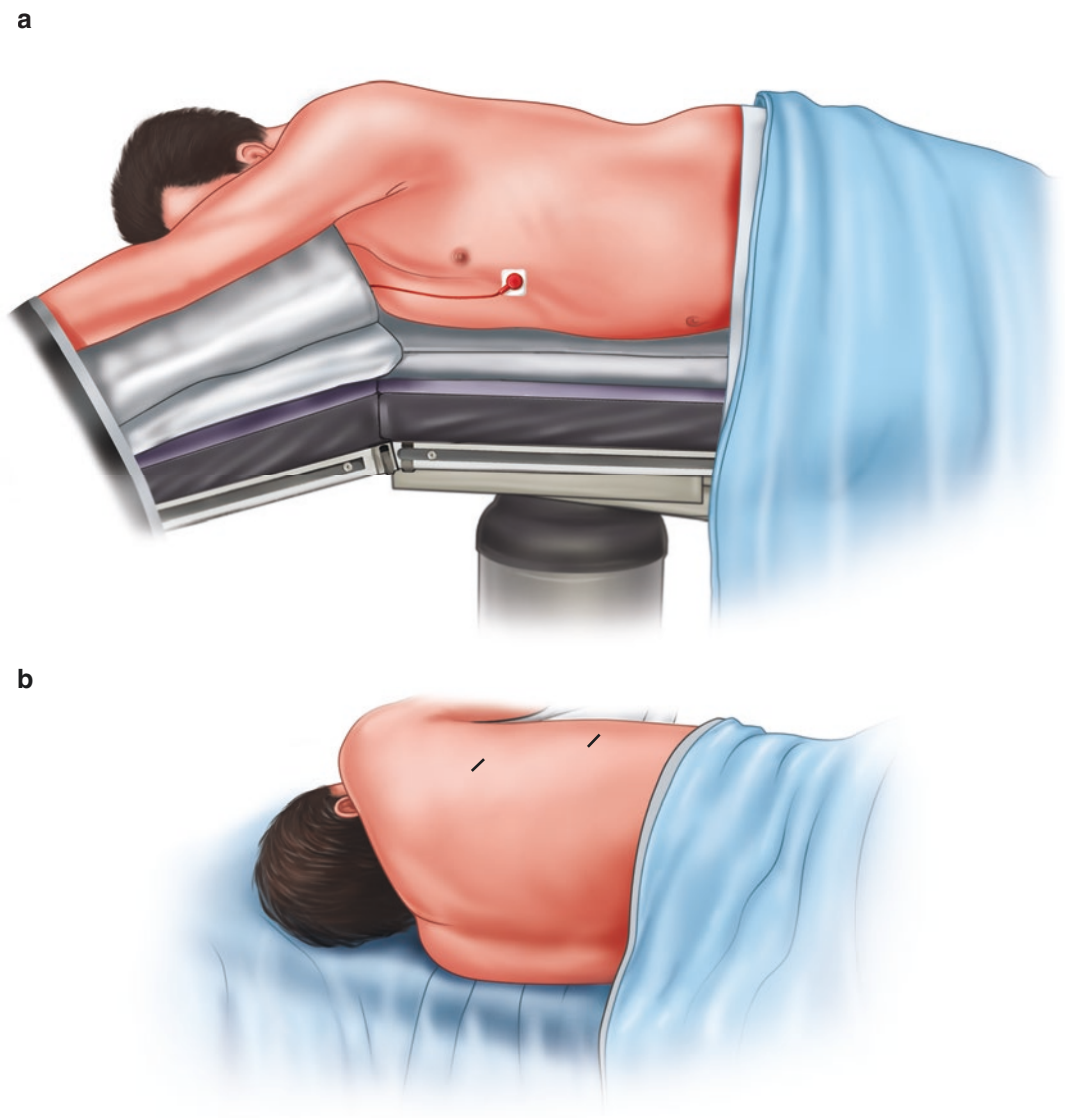


Figure 5.4

A supine position with a roll placed beneath the back on the operative side for 10°–15° elevation also can be used. The *inked lines* denote port placement

Figure 5.5

Dissection on the right side begins by incising the mediastinal pleura just medial to the right internal thoracic vein

Figure 5.4

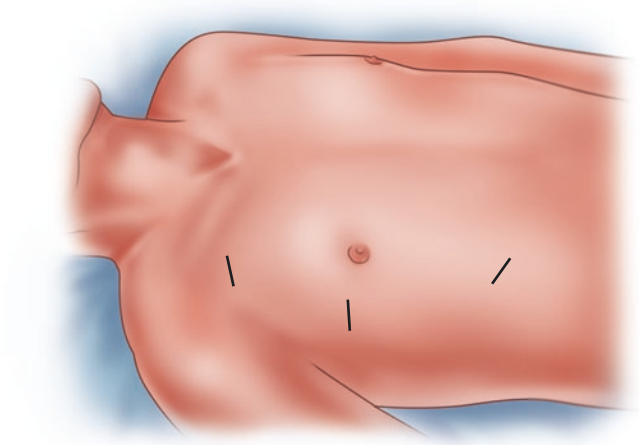


Figure 5.5

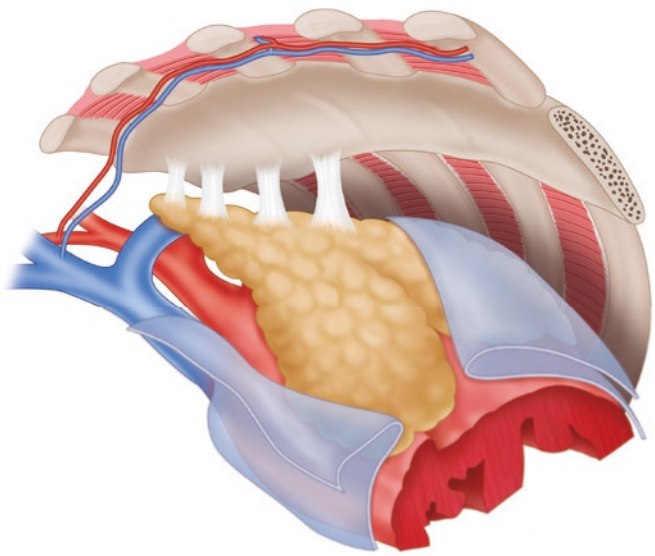


Figure 5.6

The anterior mediastinal pleura is incised, allowing the mediastinum to fall away from the sternum, providing exposure and a working area

Figure 5.7

The gamma probe has been introduced through a 10- to 12-mm thoracic port incision and scans the mediastinum. After the specimen is excised, the gamma probe can confirm the presence of the parathyroid adenoma by a high count level

Figure 5.6

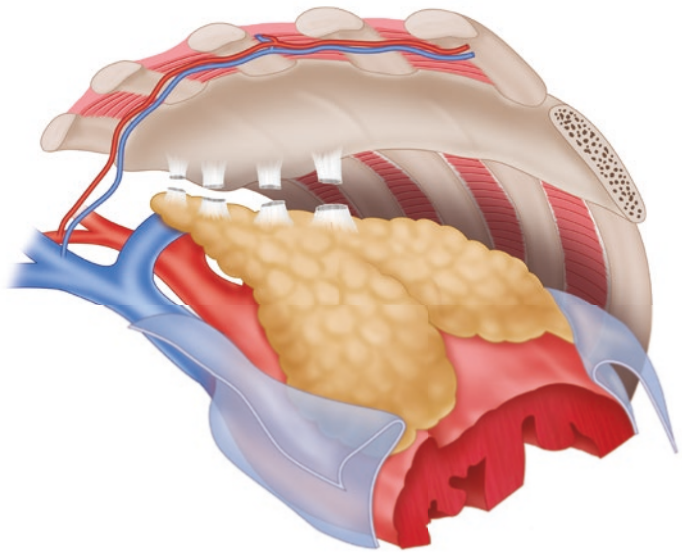


Figure 5.7

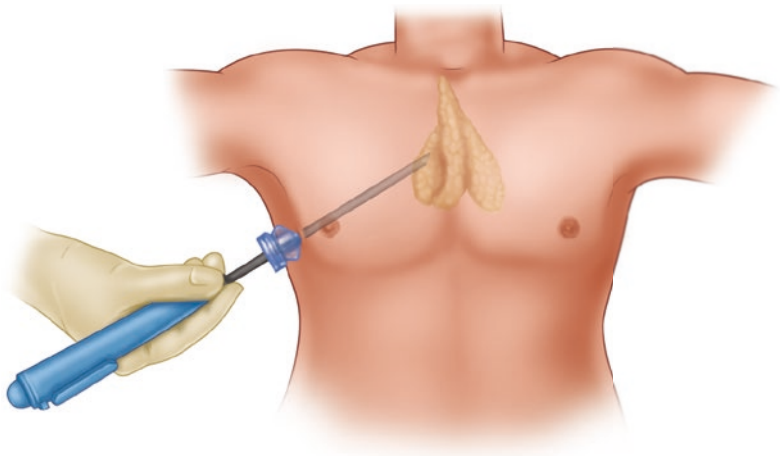
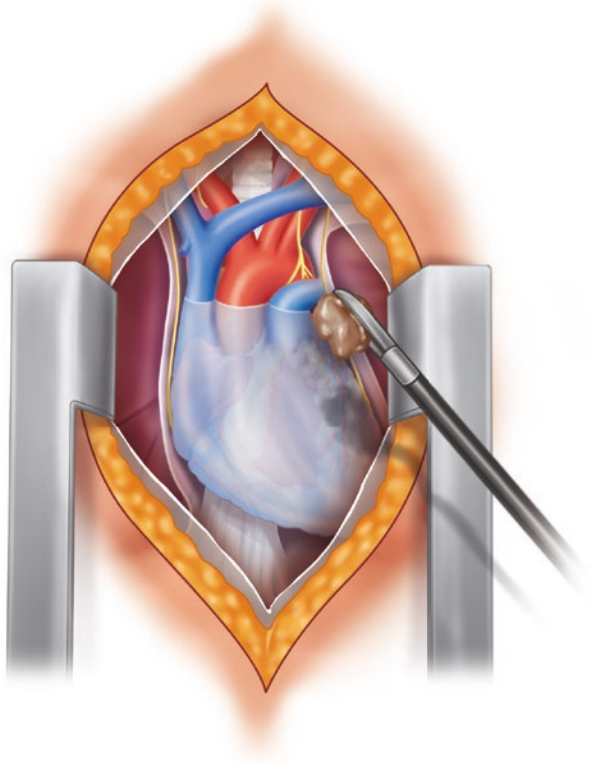


Figure 5.8

To ensure complete resection, the enlarged parathyroid gland is removed with a 1- to 2-cm rim of surrounding mediastinal fat

Figure 5.8



5.6 Anterior Mediastinotomy (Chamberlain Procedure)

The patient is placed supine and a 5- to 6-cm lateral incision is made from the lateral sternal border along the 3rd or 4th costal cartilage. The pectoralis is divided with electrocautery. The intercostal muscles are detached off the 3rd or 4th rib superiorly. Care must be taken to identify and preserve the internal thoracic vessels, which typically are located within 1 cm of the lateral sternal border. Excision of the 3rd costochondral cartilage may be necessary for exposure. Surrounding vascular structures should be clearly identified prior to identification and resection of the ectopic parathyroid. The parathyroid adenoma can be recognized by its reddish brown color, which is distinguishable from the mediastinal fat. This procedure allows the surgeon to both see and feel the abnormal gland, but it is certainly more painful than VATS.

5.7 Complications

Median sternotomy in patients with hyperparathyroidism and osteoporosis carries a high morbidity, with complication rates of up to 29%. Russell et al. [12] reported 38 patients who underwent median sternotomy for hyperparathyroidism. Chest complications, including pleural effusion, pneumothorax, and pneumonitis, occurred in eight (21%). Three patients (8%) had wound complications, including a hematoma, sternal dehiscence, and anterior mediastinitis. Conn et al. [11] reported a 19% complication rate (4 of 21 patients), including a subclavian vein thrombosis, chondritis of the xiphisternal junction, and pleural effusions in two patients. Pulmonary sequelae, sternal wound complications, major vascular injury, and phrenic and recurrent laryngeal nerve injuries also have been described [10, 13].

Anterior mediastinotomy may be performed with far less morbidity. Ravipati et al. [13] described 10 patients who underwent anterior mediastinotomy (Chamberlain procedure) for parathyroidectomy, through a small anterior thoracotomy incision made at the level of the costal cartilage nearest to the parathyroid adenoma. They had no postoperative complications except transient hypocalcemia in one patient. Wells and Cooper [14] described a technique of closed anterior mediastinal exploration. This procedure, called an extended cervical thymectomy, uses a special retractor to elevate the sternum to facilitate removal of the thymus through a cervical incision. This approach is not applicable for glands located in the posterior mediastinum, aortopulmonary window, or pericardium, however. In patients who have an extremely high perioperative risk, angiographic embolization is an option. Angiographic ablation of thoracic parathyroid adenomas was originally achieved through high-pressure injection of contrast material. Embolizations are now performed by injecting small particles or Gelfoam to occlude the feeding vessel of the parathyroid gland, resulting in ischemia, but this technique is associated with a high failure rate of approximately 40% [15]. The largest series was reported by Doherty et al. [16], performing 30 ablations in 27 patients. Normocalcemia was obtained in 14 patients (52%). Three patients (11%) were hypocalcemic after the procedure, and 10 patients (37%) required further intervention [17].

For lesions located below the innominate vein, we prefer a thoracoscopic approach for parathyroidectomy. Minimally invasive thoracoscopy/VATS procedures avoid the morbidity of sternotomy or posterolateral thoracotomy, resulting in decreased pain and a shorter hospital stay. Because of the rarity of this disease, most thoracoscopic parathyroidectomies have been reported as small case series [22]. VATS parathyroidectomy carries an approximately 7% complication rate. Reported complications include pulmonary problems such as pleural effusions, recurrent laryngeal nerve palsy, dysphonia, and hypocalcemia [18]. The largest single series was reported by Randone et al. [19], who described 13 patients undergoing VATS parathyroidectomy. No perioperative deaths or major complications occurred in their experience. Mild complications (pneumothorax and temporary recurrent laryngeal nerve palsy) occurred in two patients (15%). More recently, use of the *da Vinci*® robot (Intuitive Surgical, Sunnyvale, CA) for assisted thoracoscopic mediastinal parathyroidectomy has been described, and identification of the adenoma and resection were successful in at least in one patient in whom traditional thoracoscopic instrumentation could not visualize the lesion [23].

5.8 Conclusions

About 2% of mediastinal parathyroid glands will not be amenable to a cervical approach for resection. Minimally invasive thoracoscopic/VATS resection may be performed with less morbidity than a sternotomy or posterolateral thoracotomy. In certain patients, anterior mediastinotomy may offer a direct approach with lower morbidity than a sternotomy or thoracotomy. Preoperative localization and intraoperative PTH monitoring are crucial to a successful outcome.

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Part II

Thyroid

Thyroid Lobectomy and Total Thyroidectomy

6

Ashok R. Shaha

The incidence of thyroid cancer has almost quadrupled over the last quarter of a century. In 1975, we used to see 8000 new patients with thyroid cancer, whereas today we see approximately 66,000 new patients with thyroid cancer in the U.S. [1]. The majority of these cases are directly related to incidentalomas i.e., nonpalpable nodules, incidental findings of thyroid nodules on routine clinical examination, imaging studies such as ultrasound, carotid Doppler studies, and CT scans or MRIs performed for other cervical problems. Appropriate evaluation of the thyroid mass includes a dedicated ultrasound of the thyroid with recognition of the suspicious features, such as hypervascularity, irregular margins, and punctate calcification. After initial clinical evaluation and ultrasound examination, the patient is generally advised to have a fine needle aspiration biopsy. The results of the biopsy are used to determine whether the patient requires surgical intervention or close monitoring and follow-up. If the needle biopsy is suspicious for or proves to be cancer, the patient will require surgical intervention.

Diagnostic thyroid lobectomy is performed for patients in whom the fine needle aspiration biopsy is reported to be atypical, such as in Hurthle cell lesion or follicular neoplasm (Bethesda type III or IV). Appropriate evaluation of the opposite lobe is critical prior to consideration of the extent of thyroidectomy. However, a small percentage of patients who undergo diagnostic thyroid lobectomy may need completion thyroidectomy at a later date if the final pathology report shows this to be aggressive thyroid cancer. Advances in technology and molecular biology have helped us to further our diagnostic acumen, with additional tests such as *BRAF, RET, NRAS*, and *KRAS* mutation analysis, PAX-8/PPAR rearrangement, and the Afirma genetic expression classifier [2]. These tests are quite helpful in selecting patients in whom the decision to have surgery is important, especially in young women who may not want a scar on their necks. There continues to be a strong debate about the extent of thyroidectomy, and whether this should be lobectomy or total thyroidectomy. The decisions about the extent of thyroidectomy are best made in the operating room based on gross findings at the time of surgery, preoperative evaluation with needle biopsy, the status of the opposite lobe, the size of the suspected tumor, the status of the neck nodes, and the possibility of requiring radioactive iodine (RAI) in the future.

If there are gross abnormalities on the opposite lobe or the patient is likely to require RAI based on the initial extent of the malignancy, it is most appropriate to consider total thyroidectomy at the outset. Clearly, the complications of thyroid surgery are directly related to the extent of thyroidectomy and inversely proportional to the surgeon's experience. There is considerable debate about the number of procedures surgeons should be performing, but those doing more than 30–50 thyroidectomies a year are generally considered to have adequate volume [3].

6.1 Indications for Surgery

The major indication for surgery includes a thyroid nodule that is suspicious or atypical on needle biopsy or when the diagnosis of malignancy has been confirmed preoperatively. The decision about extent of thyroidectomy, i.e., lobectomy or total thyroidectomy, should be based on discussions with the patient, the endocrinologists, and the long-term follow-up plan. Diagnostic thyroid lobectomy is commonly performed for atypical fine-needle aspiration biopsy. The incidence of thyroid cancer is much higher in patients with thyroid nodules greater than 3 cm, and most of these patients will require surgical intervention both for diagnostic and therapeutic purposes even if the needle biopsy is inconclusive. Clinical findings such as a hard thyroid nodule, a fixed nodule, the presence of hoarseness of voice or vocal cord paralysis, tracheal deviation, and suspicious nodal metastasis are strong indications for surgical intervention, since the risk of malignancy is quite high in this group of patients.

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J.R. Howe (ed.), *Endocrine and Neuroendocrine Surgery*, Springer Surgery Atlas Series, DOI 10.1007/978-3-662-54067-1_6

6.2 Preoperative Work-Up

The preoperative work-up includes standard thyroid function tests to make sure the patient is euthyroid, checking preoperative calcium levels to rule out simultaneous hyperparathyroidism, and employing thyroid antibodies to rule out Hashimoto thyroiditis. The incidence of complications in patients with hyperthyroidism or with Hashimoto thyroiditis is quite high, and it is important to know about these pathologies preoperatively, both to prepare the patient for a slightly higher incidence of complications and to consider total thyroidectomy. In these individuals the opposite lobe is generally heterogeneous and may develop thyroid nodules in the future. A preoperative flexible laryngoscopy or mirror examination is crucial to evaluate the function of the vocal cords. Preoperative vocal cord palsy will indicate the locally advanced nature of the thyroid cancer, and appropriate cross-sectional imaging would be important to evaluate the extent of the disease and the proximity of the thyroid gland to the vital structures in the central compartment of the neck. It is also helpful to know if there is a paralysis of one vocal cord so that one can be absolutely sure to protect the opposite recurrent laryngeal nerve and to perform an oncologically sound surgical procedure with resection of the recurrent laryngeal nerve on the side of the paralysis. Generally, patients with vocal cord paralysis may have pathologically aggressive thyroid cancers such as the tall cell or insular variety.

Preoperative ultrasound of the thyroid is important to evaluate the extent of the disease and the status of the lymph nodes both in the central compartment and in the lateral neck. The lateral neck evaluation by ultrasound is considered important to identify abnormal lymph nodes preoperatively in the lateral neck so that they can be appropriately evaluated and resected at the time of surgery. In the presence of the thyroid gland, the central compartment lymph nodes are difficult to evaluate. However, if there are any suspicious lymph nodes noted on preoperative ultrasound, appropriate attention should be paid to the evaluation of the central compartment nodes ipsilaterally or bilaterally. Performing CT scans with contrast meets with considerable resistance because the iodinated contrast material delays the RAI ablation for a period of 2–3 months. However, such delay is unlikely to have any major effect on management. CT scans can definitely help the operating surgeon to evaluate the extent of the disease preoperatively, the status of the lymph nodes in the lateral neck and evaluate the parapharyngeal, retropharyngeal, and superior mediastinal areas, which are difficult to image with routine ultrasound of the neck. The CT scan should be critically reviewed to rule out retroesophageal innominate artery (arteria lusoria) with nonrecurrent laryngeal nerve. MRI is another cross-sectional imaging modality with utility, but we generally prefer a CT scan with contrast. PET scans are rarely necessary unless the patient has a very advanced stage cancer of the primary tumor with bulky nodal disease, suspicious distant metastasis, or recurrent thyroid cancer.

6.3 Preoperative Discussion and Consultation

It is important to discuss with the patient and the family the extent of thyroidectomy, lobectomy versus total thyroidectomy. This decision is based on preoperative ultrasound, size of the tumor and other diagnostic results. The final decision is best made in the operating room based on gross findings, the status of the opposite lobe, and possible nodal metastasis. Generally the procedure should begin on the diseased side first. If there is any concern about the nerve function, the procedure may need

to be terminated after lobectomy alone. A thorough discussion with the patient and the family should be carried out related to the complications of surgery such as scarring, hematoma, re-exploration, hoarseness of voice, inability to raise the voice, the need for thyroid medication, and calcium and vitamin D supplementation. Patients should be aware of the possibility of change of voice and inability to project the voice, which may have direct implications for professionals such as lawyers, teachers, singers, and others who use their voice for their livelihood. The majority of patients today are well-read and well-prepared from Internet searches to understand the procedure. However, every opportunity should be given for them to ask questions preoperatively. The complications related to hematoma requiring emergency re-exploration should also be discussed, even though its incidence is quite low.

Bilateral vocal cord paralysis leading to airway problems or tracheostomy is a rare complication but should be discussed in high-risk patients, especially those presenting with primary bulky tumors, or when one vocal cord is paralyzed preoperatively. Specific complications related to neck dissection, such as accessory nerve weakness, inability to raise the shoulder, excessive chyle drainage, and extended hospitalization, along with Horner syndrome, should be discussed. Horner syndrome with asymmetry of both eyes may be hard for a young woman to accept because of emotional and cosmetic concerns.

6.4 Anesthesia

Most thyroidectomies are performed under general anesthesia; however, some surgeons may consider performing it under twilight anesthesia without intubation and with regional block. The operating surgeon and anesthesiologist must be familiar with regional block and continuous propofol sedation. Some surgeons prefer this so that the patient can verbalize during surgery to evaluate his or her vocal cord function. Performing surgery under local anesthesia requires previous experience and expertise, since such patients may become claustrophobic once the drapes are placed on the face. Blood type and cross-matching are rarely necessary; however, some institutions preserve a sample of blood in the blood bank in the event that any life-threatening emergency occurs. Most patients can be easily intubated with a standard technique of anesthesia, paralysis, and intubation. Intubation for thyroidectomy should be attempted with a No. 6 or 7 tube to avoid intratracheal friction injury. The larger tubes are not necessary for thyroidectomy because they may cause more trauma to the endolarynx and vocal cords. Intubation should be performed by a senior member of the anesthesia team avoid any intubation related trauma or arytenoid injury and dislocation. Thyroid surgery may be performed with laryngeal mask anesthesia (LMA). However, this will be dictated by the practice of the institution and the operating surgeon. Patients should be paralyzed during the surgical procedure to avoid any coughing or bucking in the middle of the surgical procedure, which may lead to trauma to the endolarynx. The cuff of the endotracheal tube should be way below the vocal cords. If the anesthesiologist is going to use a glide scope, the position of the endotracheal tube and cuff can be easily confirmed. This is more crucial if the nerve integrity monitor (NIM) technique and a special NIM tube are going to be used. With the NIM monitor the patient cannot be paralyzed, so that one can check for nerve stimulation during surgery.

6.5 Position of the Patient and the Incision

The incision should be marked to conform to the neck crease when the patient is sitting in the office or in the holding area near the operating room. In young women, it is better to place the incision higher up. However, in general the incision should be very close to the cricoid cartilage area (Fig. 6.1).

The length of the incision should be determined based on the extent of the surgical procedure, the patient's size, the neck configuration, and the extent of the disease. If the patient is likely to need neck dissection as the first procedure or in the future, the incision should be placed close to the

Figure 6.1

The incision may be placed just below the cricoid cartilage, conforming to the skin crease. If the patient is likely to require neck dissection, a higher incision on the cricoid cartilage is preferred rather than making an apron-shaped incision

Figure 6.2

The patient's neck is extended on the head plate of the operating table. A shoulder rest is preferred for best extension of the neck

cricoid cartilage. This position gives the best exposure to the entire neck and the J-shaped or the apron-shaped incision can be avoided. Although cosmetic concerns should be kept in mind, the operating surgeon needs to remember that exposure is the most important factor in completeness of resection in thyroid cancer, which is a key factor in the best control of cancer. The position is a standard supine position with the arms padded and tucked and with the shoulder resting on three flat sheets to support the scapula and to extend the neck (Fig. 6.2). The neck should be stabilized with a doughnut, and the incision generally marked and then infiltrated with lidocaine and epinephrine. Approximately 1 mL of the solution should be used to avoid excessive bleeding from the skin and the subcutaneous area.

Figure 6.1

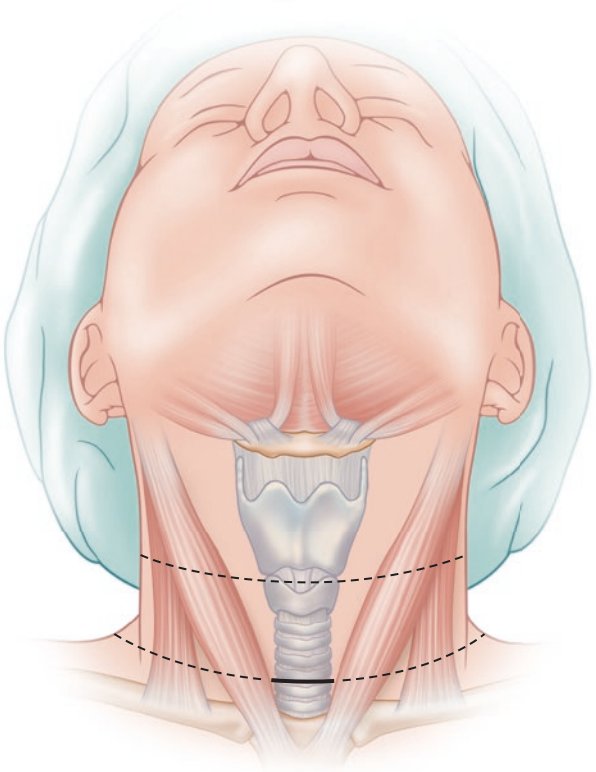
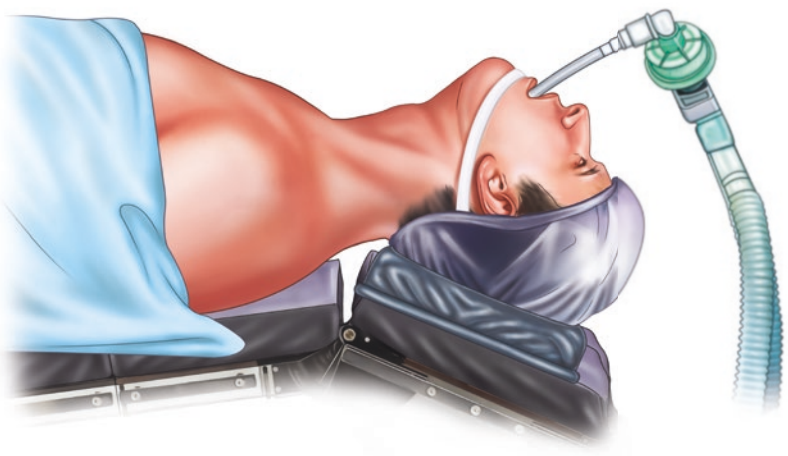


Figure 6.2



6.6 Surgical Procedure

The skin should be incised with a knife. After the skin incision, most of the dissection is performed with electrocautery. Unipolar cautery is commonly used. Initially, the subcutaneous tissue should be incised with pointed electrocautery, and subsequently a flat electrocautery should be used. The skin and subcutaneous tissue are incised. The platysma is then incised. There is hardly any platysma in the midline, and the platysma can be seen as a well-developed muscle in its lateral potion. The upper flap should be raised under the platysma by elevation with skin hooks where an essentially avascular plane can be raised under the platysma (Fig. 6.3). The upper flap should be raised up to the thyroid notch, and the lower flap taken down to the sternal notch. At this time, the midline fasciae is exposed, and this should be incised with electrocautery. Occasionally, there are communicating veins between the two anterior jugular veins, which should be cauterized, ligated, or divided with a harmonic scalpel or LigaSure energy device. The strap muscles should be separated in the midline. Opening this area can be compared to opening a "gift box," with the thyroid situated under the gift wrap, covered by strap muscles and the fascia [4]. The anterior strap muscles (sternohyoid) can be easily separated and pulled laterally. Rarely, this may require transection for better exposure if the tumor is adherent to the strap muscles. There is a debate about cutting of the inner strap muscle (sternothyroid). When necessary, we generally prefer to cut the inner strap muscle superiorly both from an oncologic point of view and for better exposure of the superior thyroid pole. The sternothyroid may be cut above and below for better exposure of a thyroid tumor. At this time, the dissection is performed on the lateral side of the thyroid. The middle thyroid vein is identified, and is clamped, ligated, and cut, or an energy device used. Gentle dissection may be performed in the inferior portion to expose the tracheoesophageal groove in this area.

The upper pole is now exposed. A clamp is placed on the upper portion of the thyroid lobe, and the thyroid lobe is pulled inferiorly and laterally; this opens up the medial aspect of the superior thyroid vessels known as Joll's triangle. There are always tiny veins in this area from the superior thyroid vein, which should be cauterized. At this juncture, the superior thyroid vessels are pulled inferiorly and laterally, which may expose the superior laryngeal nerve (Fig. 6.4). If the nerve can be identified, it is pushed up and medially and preserved carefully by ligating the superior thyroid vessels inferior to the superior laryngeal nerve. Quite often the superior laryngeal nerve may be difficult to identify, and the superior thyroid vessels should be clamped, ligated, and cut or an energy device to divide it very close to the upper pole of the thyroid. There are always minor veins with multiple branches from the superior thyroid vessels, which should be carefully ligated or cauterized. At this time, the dissection continues from the superior pole on the lateral side. On the right side, due consideration should be given at this time to evaluate if the patient has a nonrecurrent laryngeal nerve. The dissection is performed on the lateral side of the thyroid gland, exposing the entire thyroid lobe and pulling it medially. We generally prefer finger retraction of the thyroid lobe and dissection into the paratracheal area; however, some surgeons prefer using an Allis or Lahey clamp on the thyroid, although this may cause capsular trauma and bleeding from the thyroid gland. The surgeon's hand-retraction probably gives the best nontraumatic exposure of this area. The dissection may be continued in the medial aspect of the superior thyroid pole, where the pyramidal lobe may be identified. There is always a tiny vein in front of the cricoid cartilage, which should be ligated. This vein is important because if it is not identified it may cause postoperative bleeding when the patient coughs or bucks at the end of the surgical procedure. As the superior pole and the lateral aspect of the thyroid are exposed, the tracheoesophageal groove area should also be exposed. The parathyroid glands can be identified in the superoinferior portion of the thyroid gland in front of and behind the recurrent laryngeal nerve (Figs. 6.5 and 6.6). Occasionally, the parathyroid glands may be in the thyroid capsule, which requires careful dissection and separation of the thyroid from the parathyroid gland. Every effort should be made to carefully preserve the vasculature of the parathyroid gland, and separating them intact is important (Fig. 6.6) [5]. If a parathyroid gland appears to be devascularized, it should be auto-transplanted into the sternocleidomastoid muscle after confirming that it is parathyroid tissue on frozen section from a small biopsy. It is important to avoid implantation of lymph nodes or metastatic thyroid carcinoma. As the dissection continues on the lateral aspect of the thyroid, the area of the tuberculum Zuckerkandl is identified.

The recurrent laryngeal nerve is generally posterior to the tuberculum Zuckerkandl, which can be easily identified by the retraction of the tuberculum. The recurrent laryngeal nerve may be identified in three distinct areas. First, in the tracheoesophageal groove and traced in its entirety up to the

cricoid cartilage. This is where it is more commonly found when evaluating suspicious lymph nodes. The second region where the nerve can be found is its crossing on the inferior thyroid artery. However, it must be remembered that in approximately a quarter of the patients, the nerve may be in front of the inferior thyroid artery and not behind it (Fig. 6.7). Our current practice is to find a short segment of the nerve near the ligament of Berry, behind the tuberculum Zuckerkandl (Fig. 6.8).

The dissection in the region of ligament of Berry and tuberculum Zuckerkandl is quite critical, and meticulous dissection and mobilization of the thyroid should be performed. The thyroid gland is generally mobilized medially, although excessive medial retraction may cause traction injury to the nerve. This should be kept in mind at the time of transecting the ligament of Berry. Invariably, there are tiny vessels in the ligament of Berry that may cause bleeding. The bleeding should be controlled very carefully, either with electrocautery or with bipolar cautery with a fine tip forceps. If a tie is to be placed on this bleeding vessel, it should be with Vicryl or chromic catgut, which are dissolving suture materials. The inferior thyroid veins, which are generally multiple and some of which may be parallel to the recurrent laryngeal nerve or the trachea, should be carefully ligated. One may find an arteria thyroidea ima vessel in this region, which generally runs from the brachiocephalic trunk along the trachea to the inferior aspect of the thyroid. The hemostasis of inferior thyroid veins is critical, as these veins may retract into the mediastinum, causing bleeding that is difficult to control. After mobilization of the entire lobe, the dissection continues on the surface of the trachea in the pretracheal plane. The extent of thyroidectomy will depend upon the disease process and the personal philosophy of the operating surgeon. Occasionally, a small remnant of thyroid tissue is left behind in an effort to protect the parathyroids and the recurrent laryngeal nerve. However, generally we perform extracapsular true total thyroidectomy in patients with suspected malignancy. In spite of this, a small portion of thyroid tissue may be left behind near the ligament of Berry, the superior pole, and the pyramidal lobe area.

After mobilization of the entire lobe, careful attention should be paid to hemostasis and evaluation of the tracheoesophageal groove area for any obvious evidence of suspicious or enlarged lymph nodes. If there are any suspicious lymph nodes, they should be excised, frozen section findings obtained, and appropriate central compartment dissection performed. Some surgeons use prophylactic central compartment dissection, especially in high-risk thyroid cancer patients. After mobilization of the entire thyroid lobe, some surgeons may consider transecting the isthmic area before proceeding to the other side. Generally, we would leave the specimen intact and go to the other side and perform a similar procedure to achieve appropriate total thyroidectomy. Careful attention should be paid to the preservation of the parathyroid glands in patients undergoing total thyroidectomy. The parathyroid glands must be preserved with their blood supply. The branches of the inferior thyroid artery are ligated close to the thyroid and branches supplying the parathyroids are carefully preserved (*see* Figs. 6.5 and 6.6). Appropriate evaluation of the superior mediastinum is also important to evaluate for the presence of suspicious lymph nodes in this region. At the conclusion of the procedure, the wound may be irrigated with saline. However, we prefer no or minimal irrigation of the wound because excessive irrigation may cause disruption, devascularization, or accidental suctioning out of the parathyroid glands. If the parathyroid is to be autotransplanted, it should be done into the sternomastoid muscle contralateral to the tumor and the area should be marked either with a staple or a silk stitch for future reference.

Occasionally the tumor may be very adherent to the trachea, and the surgeon needs to make a critical decision about separation of the tumor from the trachea. Preoperative evaluation by clinical examination and appropriate imaging studies may give some indication of the adherence to or invasion of the tumor into the trachea. Obviously, if the tumor is invading the trachea, it will require appropriate tracheal resection in the form of sleeve resection and end-to-end anastomosis. If there is any indication of tracheal involvement, the surgeon must be prepared to undertake tracheal resection at the time of thyroidectomy. However, if there is no direct invasion of the trachea, most of the time the tumor can be shaved off the trachea. Careful attention must be paid to avoid tracheal injury or inadvertent opening into the trachea.

The tumor may be intimately adherent to the recurrent laryngeal nerve, but if the nerve is functioning preoperatively, most of the time the tumor can peeled off the nerve. However if it appears that the nerve is directly involved in the tumor and there is a possibility of leaving gross tumor behind, due consideration must be given to resect the ipsilateral nerve. Prior to resection of the functioning nerve, it is important to mobilize the opposite lobe and preserve the contralateral recurrent laryngeal nerve.

Figure 6.3

After incising the platysma, the flaps are raised in an essentially avascular plane below the platysma

Figure 6.4

Variations in the relation of the superior laryngeal nerve and the superior thyroid vessels. *Left*, The nerve may be medial to the superior thyroid vessels. *Center*, The nerve may enter the cricoid thyroid muscle above the cricoid cartilage. *Right*, The nerve may enter the muscle higher to the upper pole of the thyroid. *IC* inferior constrictor muscle, *CP* cricopharyngeus muscle, *CT* cricothyroid muscle

Figure 6.3

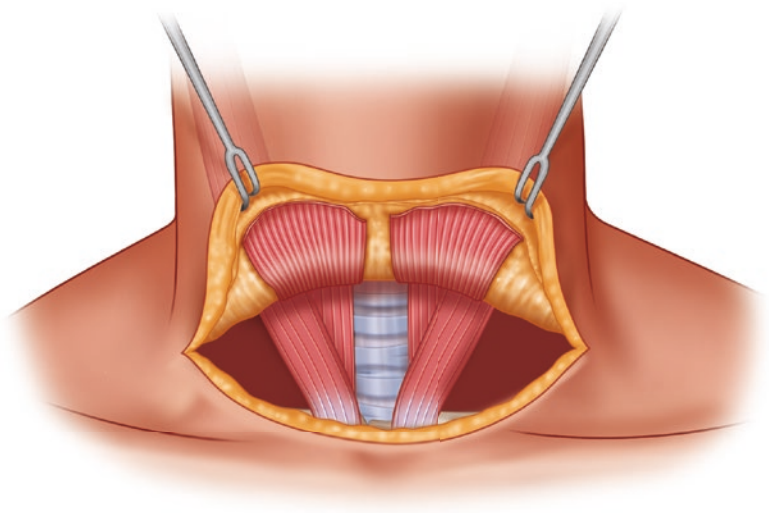


Figure 6.4

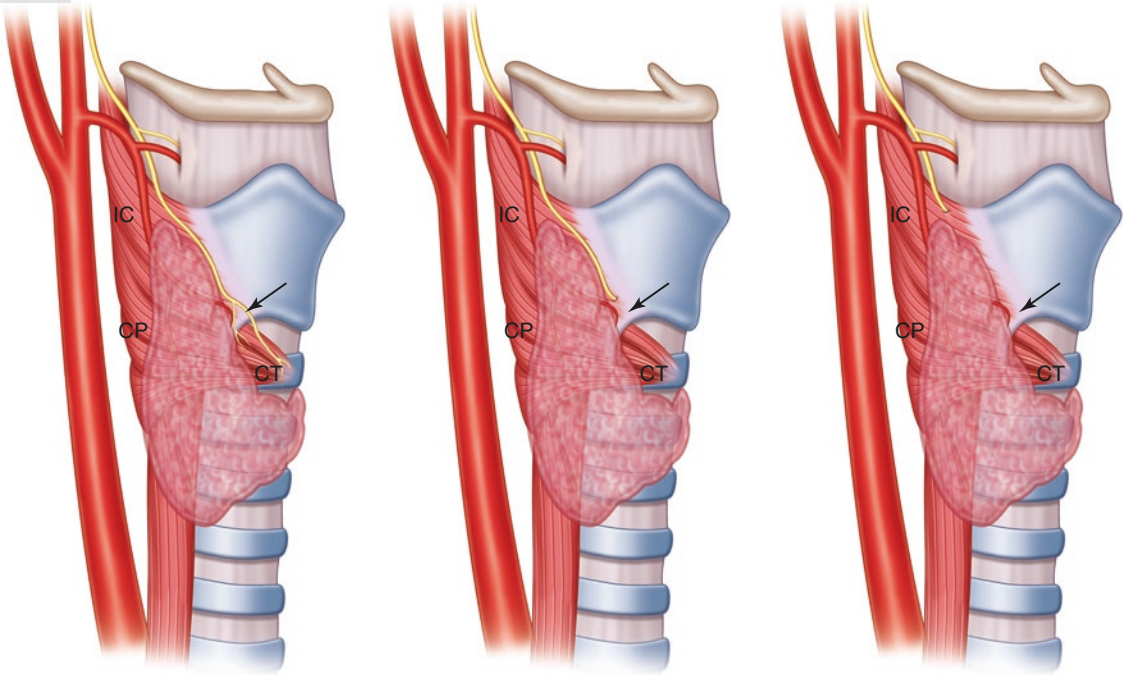


Figure 6.5

Individual ligation of the parathyroid vessels and careful preservation of the parathyroid blood supply are critical

Figure 6.6

The inferior thyroid artery directly supplies the parathyroid gland

Figure 6.5

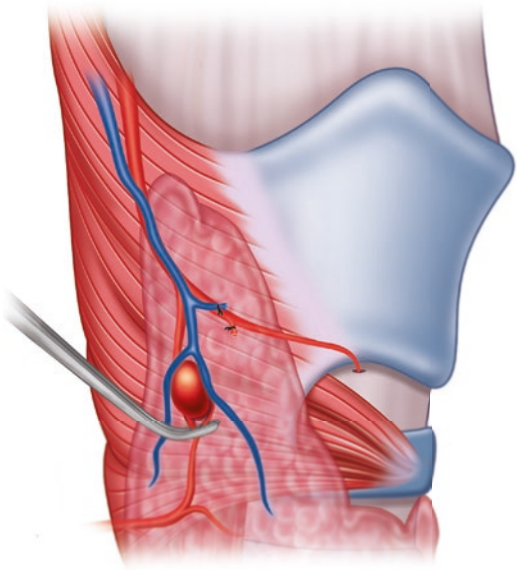


Figure 6.6

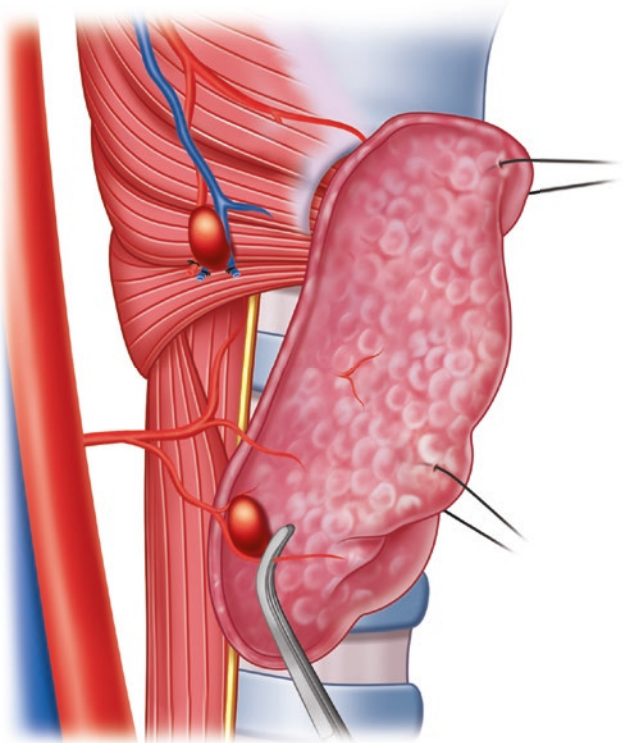


Figure 6.7

The variations in the relationship of the recurrent laryngeal nerve and inferior thyroid artery. (**a**) The nerve is behind the inferior thyroid artery. (**b**) The nerve may be in-between the branches of the artery. (**c**) The nerve may be anterior to the inferior thyroid artery

Figure 6.8

The recurrent laryngeal nerve generally runs posterior to the tubercle Zuckerkandl. *IC* inferior constrictor muscle, *CP* cricopharyngeus muscle, *CT* cricothyroid muscle

Figure 6.7

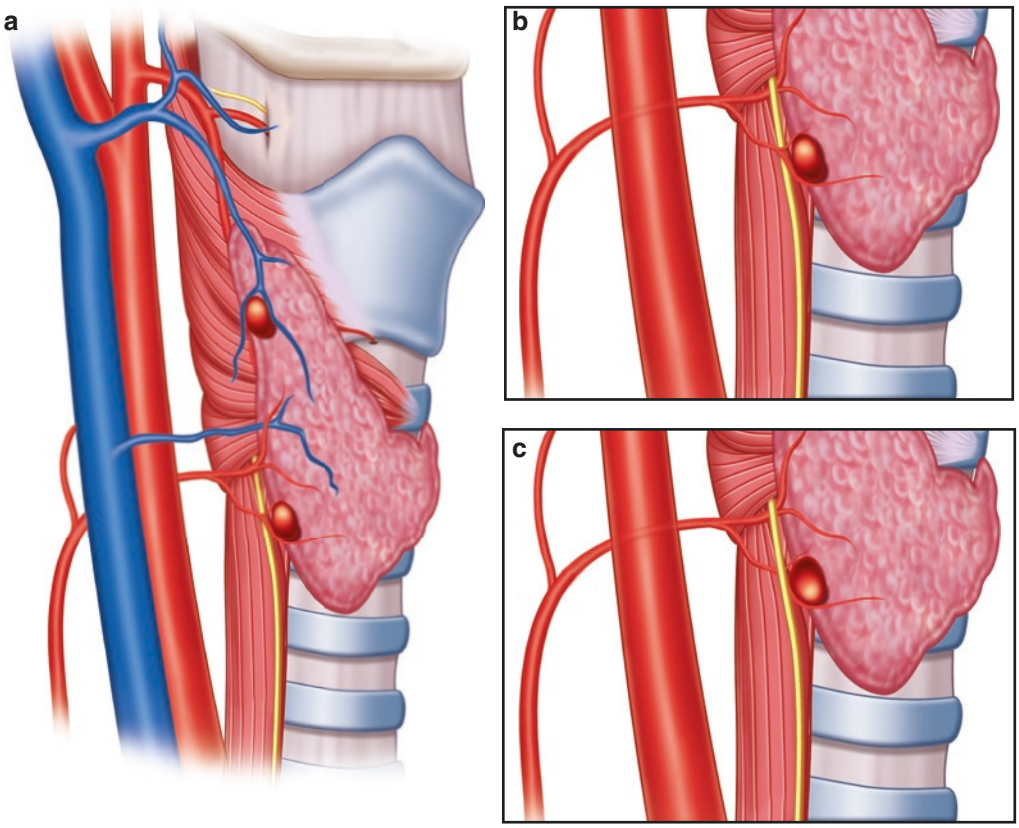
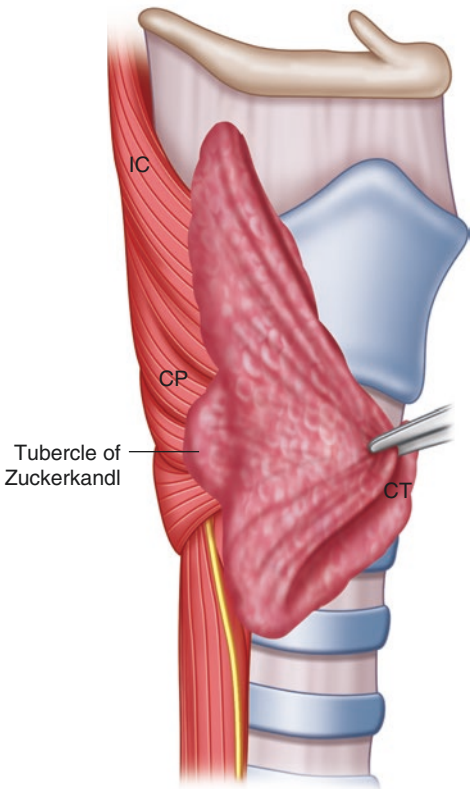


Figure 6.8



6.7 Wound Closure

At the conclusion of the procedure, the anesthesiologist is requested to perform a Valsalva maneuver to check if there are any obvious bleeding areas. After hemostasis is assured, the strap muscles are approximated in the midline with two stitches. This closure should not be water tight because it must allow the hematoma to come into the subcutaneous tissue rather than be contained behind the strap muscles, which would cause airway problems. The platysma is approximated with Vicryl stitches. The skin is closed with Monocryl stitches, and generally the wound is approximated with Dermabond. Drains are rarely used in routine standard total thyroidectomy but are commonly used in patients with large substernal goiter, those with excessive bleeding at the time of surgery, or those needing more extensive dissection such as in Graves disease or Hashimoto thyroiditis. If a drain is to be used, it should be a closed suction drain. In most cases, the drain can be removed within 24 hr and the patient can be discharged.

6.8 Intraoperative Decisions

Certain decisions need to be made in the operating room based on gross findings of the ipsilateral thyroid lobe. If the patient appears to be at high risk for thyroid cancer with gross extrathyroidal extension or a large tumor, total thyroidectomy should be performed. The central compartment should always be evaluated for any suspicious lymph nodes and frozen sections may be used generously in these patients in order to make an appropriate decision regarding central compartment dissection. If there are suspicious lymph nodes on one side, ipsilateral central compartment dissection should be performed, including levels VI and VII. The Delphian nodes are positive in approximately 20% of patients with papillary carcinoma of the thyroid, and careful attention should be paid to remove these nodes [6].

Thyroid surgery may be difficult to perform in patients with Hashimoto's thyroiditis or Graves' disease. Patients should be informed of the higher risk of complications, such as temporary or permanent hypoparathyroidism and recurrent laryngeal nerve injuries. In patients with large goiters, meticulous attention should be paid to avoid injury to the superior laryngeal nerve. If a tumor appears to be fixed to the surrounding structures, the strap muscle should be resected for better oncologic margins. We generally resect the sternothyroid muscle both for better exposure of the superior pole and for a better oncologic result. If the tumor is adherent to the trachea or the esophagus, appropriate shaving of the tumor off of these structures should be performed. If there is any suspicion preoperatively of this problem, appropriate preoperative evaluation and imaging should be performed to decide whether the patient requires tracheal resection. Tracheal resection is reserved for patients with direct invasion of the trachea where up to four to five rings of trachea can potentially be resected with end-to-end anastomosis.

6.9 Postoperative Management

The majority of patients recover very well after thyroid lobectomy or total thyroidectomy. Serum calcium levels should be checked both 6 and 23 h after the surgery and the trend of calcium levels should be scrutinized to determine the amount of calcium supplementation needed. Some institutions use parathormone (PTH) levels for evaluation of parathyroid dysfunction. Patients need to be carefully monitored in the postoperative period for symptoms of hypocalcemia and appropriate replacement as needed with calcium and vitamin D. The overall incidence of temporary hypoparathyroidism ranges between 15% and 20%. However, the incidence of permanent hypoparathyroidism is only 2%. Similarly, the incidence of temporary recurrent laryngeal nerve palsy is 4–5% but the occurrence of permanent nerve palsy is below 1%. Patients should be observed closely for any increasing swelling, airway related issues such as shortness of breath or difficulty in breathing. If there is neck fullness or an expanding hematoma, the neck wound should be opened immediately to relieve pressure. When the neck is opened, it is important to open the strap muscles by inserting a finger into the wound and evacuating the hematoma.

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Central Neck Dissection for Medullary Thyroid Carcinoma

7

J.F. Moley

7.1 Introduction

Medullary thyroid carcinoma (MTC) is a malignancy that is characterized by a high proportion of hereditary cases and secretion of the tumor marker calcitonin [1]. MTCs are moderately invasive and have a high propensity for spread to cervical lymph nodes [2]. Central lymph nodes (level VI) are involved up to 81% of the time [3, 4]. Because MTC cells do not concentrate radioactive iodine, central neck dissection is a critical component of surgical management. Total thyroidectomy and central neck dissection (TT+CND) is recommended in the initial management of the patient with MTC [4]. Lateral neck dissection in these patients is described elsewhere in this volume (Chap. 9).

The execution of this operation differs in several ways from total thyroidectomy alone. TT+CND entails fewer steps than total thyroidectomy (TT) alone because many small vessels don't need to be divided close to the thyroid to preserve the blood supply to the parathyroids. The inner strap muscle (the sternothyroid muscle) is removed en bloc with the thyroid and central neck contents on the side of the primary tumor, to ensure an adequate margin anteriorly. The surgeon must be able to identify the parathyroids, which are removed on the side of the thyroid malignancy, to be transplanted in either the sternocleidomastoid or forearm muscle, depending on the risk of subsequent hyperparathyroidism (as in MEN 2A syndrome) [5]. The parathyroids on the contralateral side may be preserved in situ, or they may be removed and transplanted. Normal parathyroids can be difficult to identify, so this procedure requires experience.

TT+CND is recommended in patients with biopsy-proven MTC. Some groups have advocated unilateral surgery (thyroid lobectomy with unilateral neck dissection), but this approach is not widely accepted [6, 7].

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The anatomic boundaries of the central compartment are the carotid arteries bilaterally, the hyoid bone superiorly, and the innominate artery inferiorly [3, 8]. In addition to the trachea and esophagus, this compartment contains the thyroid, parathyroids, thymic horn, recurrent laryngeal nerves, central neck lymph nodes, and fat.

7.2 Preoperative Workup

In addition to routine preoperative bloodwork, blood levels of calcitonin, metanephrines, and calcium should be measured in these patients.

If the patient is hoarse, or if the tumor is large, awake laryngoscopy should be done to observe cord motion and document abnormalities. If the patient has a vocal cord palsy on one side, special care must be taken with the functioning nerve, because bilateral palsies (even transient ones) usually require tracheostomy. Tracheostomy in a patient after a central neck dissection is especially dangerous because the tube is adjacent to the innominate artery with no intervening central fat, nodes, or thymus to protect the artery, and innominate blowout may occur. For patients with a vocal cord palsy on one side, consideration should be given to leaving tissue to cover the innominate artery, or to doing a unilateral procedure, in which the functioning nerve is not manipulated.

CT scans of the neck, chest, and abdomen should be done if there is evidence of significant cervical nodal involvement, or if the calcitonin level is over 150 pg/mL [4]. The presence of distant metastatic disease may influence the surgeon's choice of operation. For instance, if a patient with unilateral MTC has distant metastases and an ipsilateral vocal cord palsy, consideration may be given to performing unilateral surgery in the neck. The risk of leaving disease in the contralateral neck is increased, but unilateral surgery may be in the patient's best interest from the standpoint of quality of life.

Genetic counseling and testing for a germline *RET* gene mutation should be done but may be deferred until after surgical treatment of MTC.

J.R. Howe (ed.), *Endocrine and Neuroendocrine Surgery*, Springer Surgery Atlas Series, DOI 10.1007/978-3-662-54067-1_7

Preoperative ultrasound with marking of involved lymph nodes should be done [9–11]. Nodes with metastatic MTC have an abnormal appearance, including abnormal overall morphology, loss of fatty hilum, and calcifications. The involved nodes may be marked on the overlying skin, and the surgeon should review the ultrasound with the radiologist (or perform it, if possible) to be familiar with the findings. A permanent marker should be used, with care taken not to wash off the marks in the process of prepping.

Much has been written about the correlation between preoperative calcitonin levels and the extent of nodal involvement. It has been suggested that the preoperative calcitonin level may guide the extent of node dissection. In a study of 300 European MTC patients, nodal metastases were not identified when the preoperative basal calcitonin level was less than 20 pg/mL [12]. The basal calcitonin level was found to be correlated with involvement of nodal groups as follows:

- >20 pg/mL: ipsilateral central and lateral neck nodes
- >50 pg/mL: contralateral central nodes
- >200 pg/mL: contralateral lateral neck nodes
- >500 pg/mL: mediastinal nodes

Based upon these findings, these authors (who also wrote the European guidelines) recommend thyroidectomy alone if basal calcitonin is less than 20 pg/mL, ipsilateral central and lateral neck dissection if the calcitonin is 20–50 pg/mL, the addition of contralateral central neck dissection if the basal calcitonin is 50–200 pg/mL, and the addition of contralateral lateral neck dissection if the calcitonin is 200–500 pg/mL. Most

Figure 7.1

Positioning of the patient

experts agree that sternotomy with mediastinal neck dissection should be reserved for patients with imaging evidence of mediastinal disease. In contrast, most North American surgeons rely heavily upon preoperative ultrasound imaging to map the extent of nodal involvement and determine extent of surgery based upon calcitonin and imaging results [2, 11].

7.3 Surgical Procedure

7.3.1 Positioning and Incision

In the operating room, after the induction of general endotracheal anesthesia (which may be done with a nerve monitoring tube), the patient is placed in a mild reflex or "beach-chair" position with the head in mild hyperextension and the arms folded with the hands on the anterior superior iliac spines (Fig. 7.1). This requires pulling the draw sheet around the patient and fastening it together in the midline, creating a "papoose." This positioning is necessary because if the arms are placed at the patient's sides, there may be too much stretch on the brachial plexus, which can cause numbness and weakness of the hands and arms.

The patient is prepped from chin to upper chest and draped. The incision is made in a low collar position, ideally overlying the thyroid isthmus, using a preexisting skin crease if one is available (Fig. 7.2). Generally, this operation can be done with an incision measuring 7 or 8 cm (or less, if the surgeon is experienced). If a lateral dissection is anticipated, the incision should be longer.

Figure 7.1

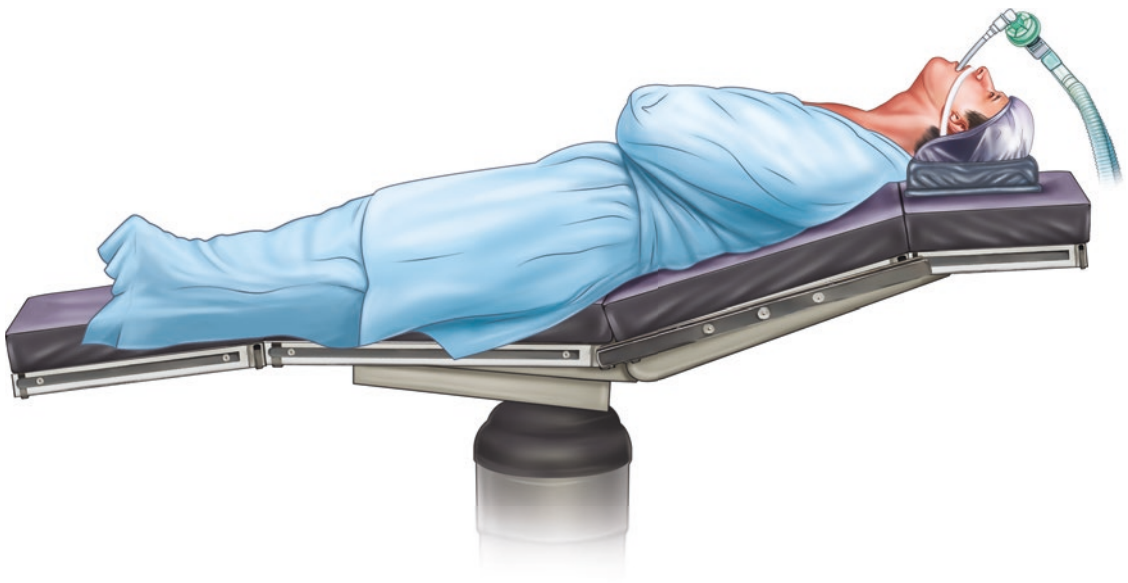
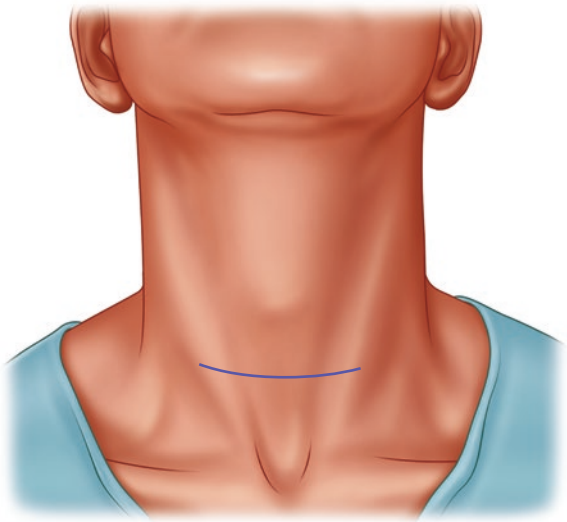


Figure 7.2

Neck incision. The length of the incision depends on whether a lateral neck dissection is also planned. If only a central neck dissection is planned, it can be done through a curvilinear low collar incision 5–10 cm in length, depending on the size and age of the patient, the extent of disease, and whether there is mediastinal extension. If possible, the incision should be place in a preexisting skin crease to achieve excellent cosmetic results

Figure 7.2



7.3.2 Initial Dissection

Subplatysmal flaps are created in the standard fashion, and a self-retaining retractor is placed (Fig. 7.3). The strap muscles are then divided in the midline (Fig. 7.4); on the side of the thyroid tumor, the sternohyoid muscle is separated from the sternothyroid muscle. The sternothyroid muscle is left attached to the underlying thyroid, and the superior and inferior attachments of this muscle are divided (at the thyroid cartilage and the sternum; Fig. 7.5).

Figure 7.3

Subplatysmal flaps have been made, exposing the anterior jugular veins and the strap and sternocleidomastoid muscles. Facelift retractors are used to elevate the flaps

Figure 7.4

Division of the plane between the sternohyoid muscles

Figure 7.3

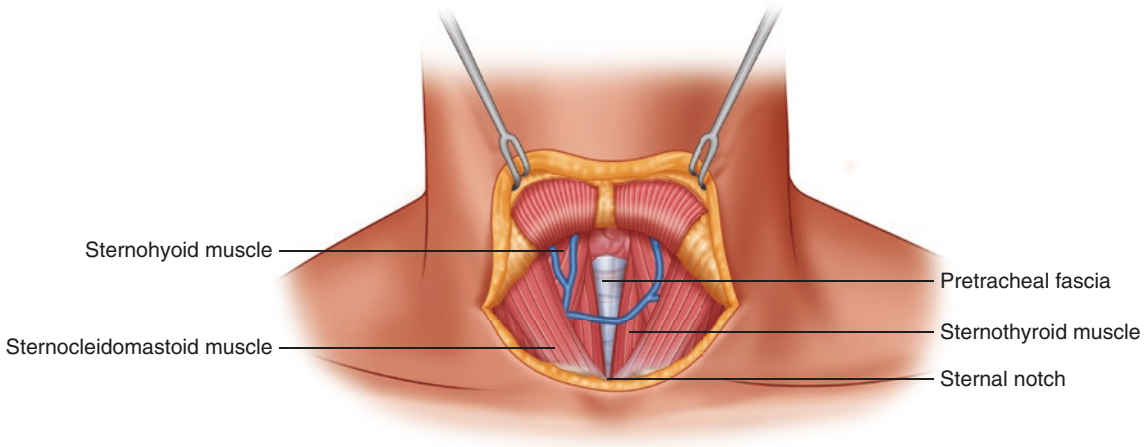


Figure 7.4

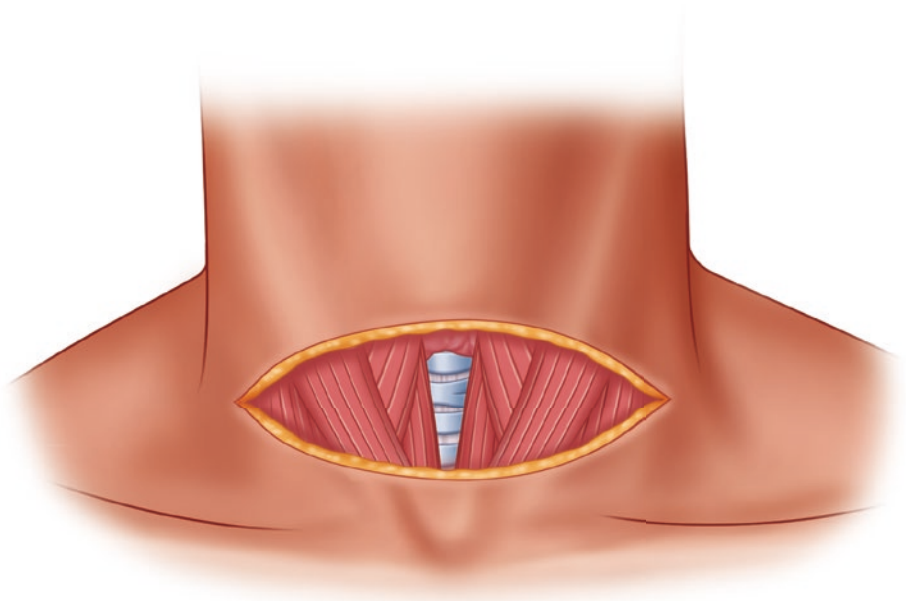
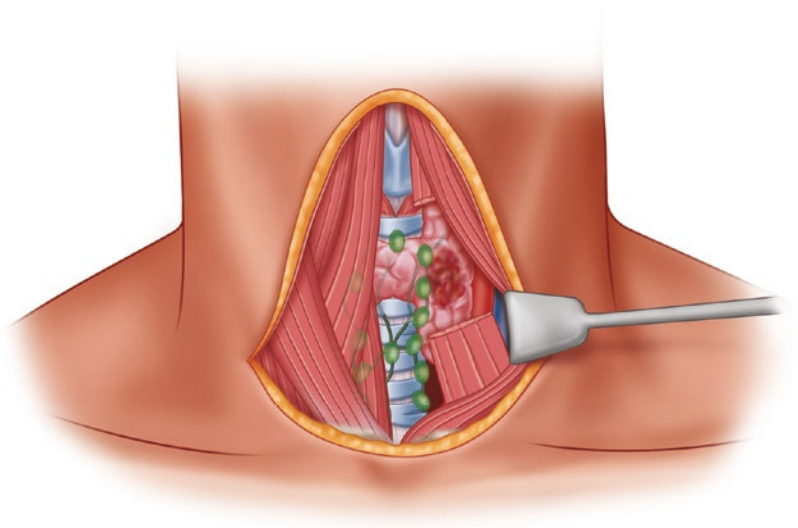


Figure 7.5

Resection of the sternohyoid muscle en bloc with the thyroid on the side of the tumor and location of central nodes

Figure 7.5



7.3.3 Thyroidectomy and Tumor Specimen Mobilization

Superior pole vessels are divided after mobilization medial to lateral to avoid injury to the superior laryngeal nerve, which may be visualized during this process. Once the superior pole is taken down, the thyroid is rolled medially and anteriorly. At this point, the procedure departs from what is done in a standard thyroidectomy. The objective is to sweep up the thyroid lobe with surrounding soft tissue and nodal tissue, leaving only the recurrent nerve behind. Attempts may be made to preserve the blood supply to the upper parathyroid, but I usually remove both ipsilateral parathyroids with the specimen, then dissect them out of the specimen if possible, and transplant them. Because I am not attempting to preserve the parathyroid blood supply on the side of the tumor, I divide the tissue on the anterior surface of the carotid artery and sweep everything medially (Fig. 7.6). This requires less dissection, with fewer vessels to control.

Dissection is carried out on the anterior surface of the carotid artery. If one stays directly on the anterior surface of the carotid, the dissection is quite safe, because the only structures encountered are the middle thyroid veins coming off the internal jugular vein; these veins should be divided. Inferiorly, as the carotid becomes the innominate, the surgeon encounters the thymic horns and associated veins overlying the trachea, which must be divided and swept into the specimen (Fig. 7.7). On the right, the dissection is done

Figure 7.6

Left central node dissection (level VI). The surgeon dissects along the left carotid and frees up the fatty tissue and nodes laterally

to the level of the innominate (brachiocephalic) artery (Fig. 7.8). On the left, the dissection is done to the level of the clavicle and left innominate (brachiocephalic) vein takeoff (Fig. 7.9) [13]. Once the central compartment contents are thus mobilized, including the thyroid, parathyroids, central neck nodes, fat, and thymus, dissection is carried out superior to inferior. For a right-handed surgeon, this dissection is generally done most easily with the surgeon on the left side, using the right hand to perform dissection from above, crossing toward the midline along the innominate artery. The thyroid is mobilized from the top down, leaving the sternothyroid muscle attached. In the process, the recurrent laryngeal nerve is identified and preserved, and the upper and lower parathyroids are identified. I generally leave the parathyroids with the specimen, remove them after removal of the specimen, place them in cold saline, and mince and transplant them as described in Chapter 4. Soft tissue and vascular attachments to the thyroid are divided, including middle veins and inferior thyroid artery and veins. The nodal packet is swept up off of the recurrent laryngeal nerve and the esophagus to the trachea. It is dissected off of the trachea, leaving only bare trachea, esophagus, and recurrent nerve centrally. Inferiorly, the specimen is swept off of the recurrent laryngeal nerve to the trachea, and the thymic horns are divided with the nodal packet at the level of the innominate artery. It is also essential to mobilize and remove the nodes that reside in the hollow behind the right recurrent laryngeal nerve.

Figure 7.6

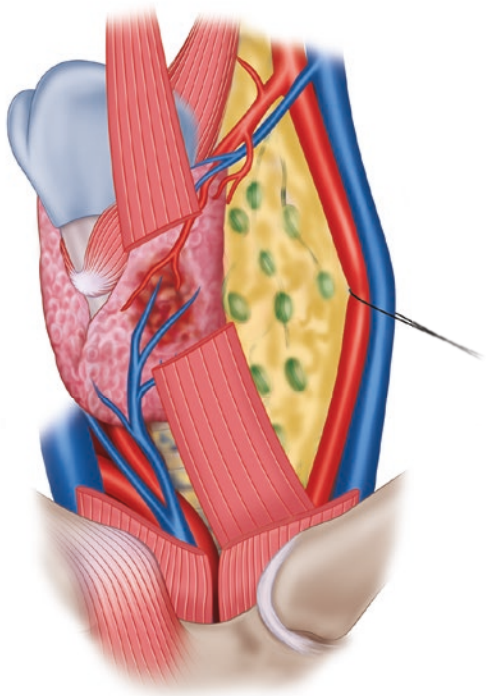


Figure 7.7

Left central node dissection (level VI). The nodes and fibrofatty tissue are dissected from the level of the hyoid bone downward along the tracheoesophageal groove to the level of the innominate vein

Figure 7.8

Right central neck dissection (level VI). The surgeon dissects along the anterior surface of the right carotid (shown partially removed for clarity), sweeping the right central nodal packet medially to be removed en bloc with the thyroid. The recurrent laryngeal nerve and vagus nerves are carefully protected

Figure 7.7

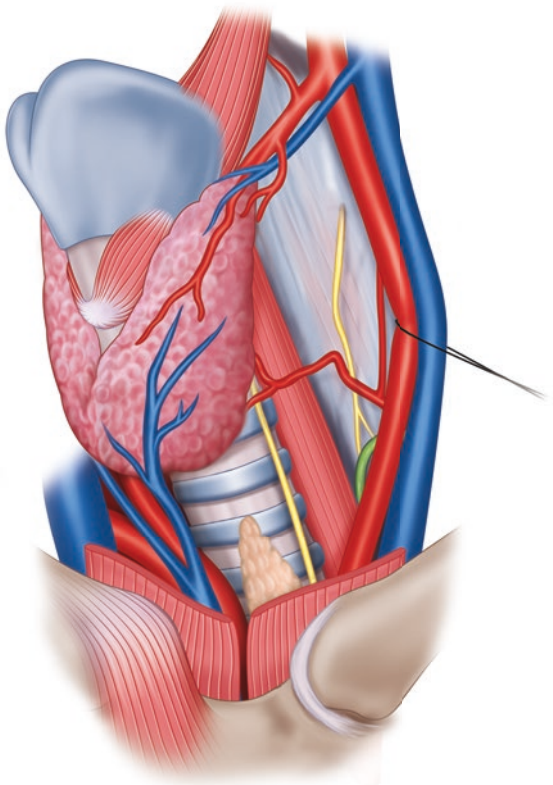


Figure 7.8

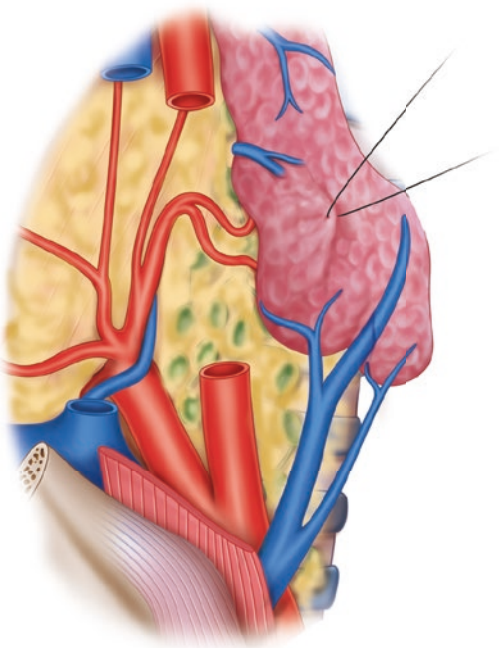
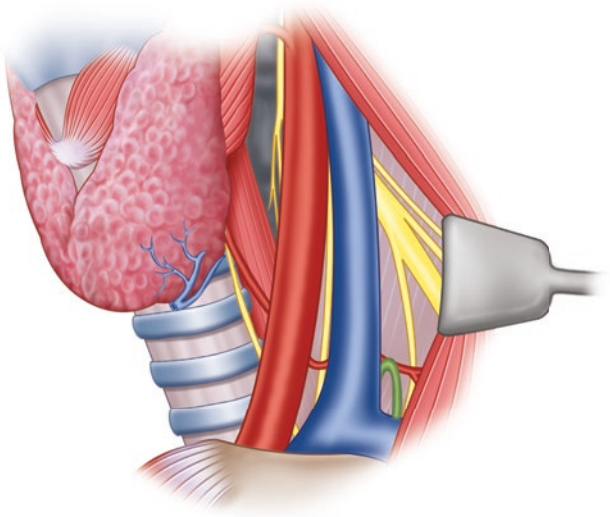


Figure 7.9

Location of the thoracic duct on the left, posterior to the carotid artery and internal jugular vein. This structure must be preserved or ligated, if injured

Figure 7.9



7.3.4 Contralateral Thyroidectomy and Node Dissection

Once the tumor side is completely mobilized, attention is turned to the contralateral side. If this side has no tumor involvement, both the sternothyroid and sternohyoid strap muscles may be mobilized off of the thyroid lobe and reflected laterally. The undersurface of the inner strap muscle is carefully cleaned off so that all fat, nodal tissue, and thymus is incorporated in the specimen. Again the thyroid superior pole is mobilized, the carotid artery is dissected on its anterior surface inferiorly, and the central compartment containing thyroid, parathyroids, nodes, and thymus is exposed (Fig. 7.8). If the surgeon prefers to preserve the parathyroids on this side, then a standard parathyroid-preserving thyroid lobectomy should be carried out, leaving the upper parathyroid on an intact vascular pedicle and the lower parathyroid on an intact pedicle in the thyrothymic ligament. Tissue

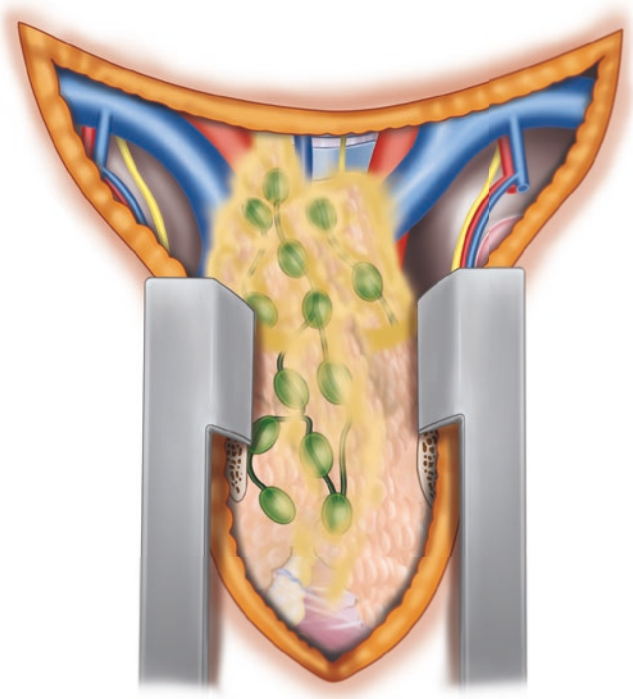
Figure 7.10

Upper mediastinal dissection (level VII) through a mini-sternotomy

medial and anterior to the thyrothymic ligament may be swept medially with the thyroid to join the contralateral dissection. The inferior extent of this packet is transected with cautery or a hemostatic device such as the harmonic scalpel, with care to ligate large veins. The entire packet including the thyroid and central neck contents is then oriented with sutures and submitted to pathology, after carefully removing any parathyroids from the tumor-bearing side of the specimen for autotransplantation.

If disease extends inferiorly into the mediastinum, it may be removed through a full or mini-sternotomy (Fig. 7.10). In the mini-sternotomy procedure, the midline sternotomy is carried down to the second or third intercostal space. Care is taken to avoid the internal mammary vessels. Dissection around the innominate vein must be done carefully. Nodal metastases are often present along the sides of the trachea as it descends deep to the innominate vein.

Figure 7.10



7.3.5 Parathyroid Autotransplantation

The ability to identify and autotransplant parathyroid glands is critically important to any surgeon who treats thyroid cancer [5, 13, 14]. Hypoparathyroidism is a preventable complication, and its incidence should be extremely low. Parathyroids that are removed during central neck dissection should be placed in cold saline, and minced into fragments of 1 × 1 mm. These fragments are then autotransplanted into individual muscle pockets (two or three per pocket) in the sternocleidomastoid muscle (for sporadic MTC and MEN 2B), or into the muscle of the of the nondominant forearm (for selected MEN 2 cases with a risk of subsequent development of hyperparathyroidism). All removed parathyroid tissue should be transplanted. Each pocket is closed with a suture. We use absorbable suture material in sporadic cases, and permanent sutures (4-0 Prolene or silk) in MEN 2A cases, in which there is a risk that the tissue may become hyperplastic and need to be located and removed in the future.

7.3.6 Drains and Closure

A drain is generally placed in the bed of the thyroidectomy and is removed after 1 or 2 days if no chyle is coming out. The straps are sutured together in the midline, the platysma is closed, and the skin is closed with a running subcuticular suture and surgical glue or Steri-Strips™. Patients usually can be discharged within 1 or 2 days.

7.4 Complications

Reoperations on the central neck have significantly higher complication rates than primary operations, and some surgeons have cited this rate as a rationale for performing the procedure prophylactically in patients with differentiated thyroid cancer, to avoid reoperative surgery in the central neck [15–18].

Complications of central neck dissection for MTC are the same as in patients with papillary thyroid carcinoma (about which much has been written recently) [8, 19]. These complications include hypoparathyroidism and recurrent laryngeal nerve injury even when surgery is performed by high-volume and experienced thyroid surgeons [19]. Permanent hypoparathyroidism results from injury to the parathyroid glands and is defined by the postoperative need for vitamin D and/or calcium supplementation at 6 months and beyond. Recent studies have suggested rates of permanent hypoparathyroidism of 1.6–16.2% following TT+CND, compared with 1.3–6.3% following TT alone [20, 21]. Judicious examination of parathyroids left in situ and carefully performed autotransplantation of removed or compromised glands results in a much lower incidence of this complication.

Permanent recurrent laryngeal nerve injury results in postoperative vocal cord paralysis or changes in vocal function that persist 6 months and beyond. Injury is diagnosed by laryngoscopy, with rates of 1.6–2.3% reported following TT+CND, compared with 1–1.3% following TT alone [20, 21]. The recurrent laryngeal nerves must be carefully identified to avoid this complication; the use of a hand-held nerve monitor may assist in management.

Temporary recurrent laryngeal nerve injury results in significant morbidity, especially in patients whose livelihood depends on their ability to speak and be heard [18, 22, 23]. The rate of this type of injury is reported to be slightly higher after TT+CND than after TT alone (5.2% vs 2.9%) [20].

There are also higher risks of clinically significant temporary hypoparathyroidism after TT+CND. The definition of clinically significant temporary hypoparathyroidism includes several aspects:

- Hypocalcemia requiring supplementation (lasting less than 6 months)
- Serum calcium concentration less than 7.0 mg/dL
- Symptoms (objectively visible muscle spasms or tetany) and/or need for intravenous replacement or calcitriol to control
- Necessity of readmission or hospitalization

It is estimated that 38% of patients experience symptomatic temporary hypocalcemia after TT, versus 64% after TT+CND [24, 25]. The overall prevalence of temporary hypocalcemia (summarized from 11 studies) was 16.2% in TT versus 31% in TT+CND [20]. Other local surgical complications have been reported to be higher in patients who had TT+CND than in those with TT alone [23, 26]. These include hematoma, seroma, chyle leak, and injury to adjacent structures including the esophagus and trachea (Fig. 7.8).

Most thyroid operations (77%) performed in the United States are not performed by high-volume specialists [27]. Several studies have demonstrated that the rates of hypoparathyroidism and recurrent laryngeal nerve complications are higher when performed by low-volume surgeons who do not specialize in thyroid surgery [28].

7.5 Results and Conclusions

Central neck dissection for MTC usually yields between 6 and 20 lymph nodes in the specimen, though higher and lower numbers may be seen depending on the thoroughness of dissection and pathologic examination [3, 8, 13]. When properly done, central neck dissection results in excellent

long-term control of MTC in the central neck, improvement in the accuracy of staging, and decreased postoperative calcitonin levels [29, 30].

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Substernal Goiter

8

Daniel Oertli

8.1 Introduction

Substernal or mediastinal goiters develop from the thyroid gland and progressively migrate into the thoracic cavity because of their weight, negative thoracic pressure, respiratory movements, and the shortness of the patient's neck. They derive their blood supply from the superior and inferior thyroid arteries, which are surgically accessible through the neck. Substernal goiters should be distinguished from ectopic goiters arising from aberrant thyroid tissue; the blood supply for ectopic intrathoracic goiters does not depend only on cervical vessels. Therefore, the surgical management of purely intrathoracic goiters differs from that of substernal goiters [1].

Substernal goiters can remain asymptomatic until compression affects the neighboring structures located at the thoracic inlet or the mediastinum. The most common symptoms are dyspnea, dysphagia, cough, and hoarseness [2, 3]. In about 10% of cases, superior vena cava compression with venous congestion of the head and neck region is reported [2]. Occasionally, vascular compression of the vertebral artery may occur, associated with syncopal episodes [4].

Most substernal goiters can be removed through a standard cervical approach even when they are associated with superior vena cava syndrome, emergent airway compression, or dysphagia [4]. In published series, manubriotomy or sternotomy for substernal goiters was required in 6–31% of cases [3–5].

8.2 Operative Technique

8.2.1 Cervical Approach

The head is reclined and the patient is positioned in a reverse Trendelenburg position at about 15–20°. Substernal goiters frequently compress veins, which may complicate surgery. By adopting this position, venous pressure is reduced. The standard incision is a Kocher incision, which is planned and marked with an indelible pen before surgery on the reclining, awake patient, following the line of a skin crease. Alternatively, the incision is marked with a thread once the patient is on the operating table. To gain good access to the substernal gland, the incision should be placed about 2–2.5 cm above the sternal notch. The incision can be extended down from the cervicotomy to the manubrium for better exposure of the thoracic inlet. This median extension of the skin incision is useful when treating large goiters; it may avoid the need to open the manubrium or the whole sternum.

The subplatysmal flaps are raised, the superficial and middle neck fascia is separated at the midline, and the strap muscles are retracted to the side. Division of the strap muscles is done selectively, especially to facilitate the transection of the upper pole vessels in patients with very large goiters.

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J.R. Howe (ed.), *Endocrine and Neuroendocrine Surgery*, Springer Surgery Atlas Series, DOI 10.1007/978-3-662-54067-1_8

First, the upper pole is prepared and resected with ligation of the superior thyroid artery and vein (Fig. 8.1). It is essential not to deliver the substernal component until these vessels have been completely ligated. By this procedure, the upper pole of the thyroid gland is mobilized, which will be important in the subsequent upward movement of the thyroid gland from the substernal position to a cervical position. Attention must be paid to the external branch of the superior laryngeal nerve, close to the superior thyroid artery. Therefore isolation of the vessels close to the thyroid capsule is crucial. The upper pole vasculature from large goiters often spreads out as it enters the thyroid gland, so clamping and suturing in several steps is usually required.

The cervical gland is further prepared, and the superior parathyroid gland and the recurrent laryngeal nerve (RLN) are routinely identified (Fig. 8.2). Visual identification may be supplemented by intraoperative nerve monitoring, a procedure that was shown to reduce transient (but not permanent) RLN paresis in a randomized, controlled trial of 1000 patients undergoing total thyroidectomy [6]. As the inferior parathyroids may be more difficult to find in patients with substernal goiters, special care must be taken to identify and preserve the superior glands. Capsular dissection, as described by Thompson et al. [7], refers to the development of a plane between the thyroid capsule and the tertiary branches of the inferior thyroid artery. The branches are ligated, clipped, or sealed directly on the capsule of the thyroid gland. This method, which is widely practiced today, minimizes surgical damage to both the parathyroid glands and the RLN.

Meticulous dissection steps will then enable the identification of the RLN where it crosses the inferior thyroid artery, as well as the two parathyroid glands. It is wise to preserve as much of the inferior thyroid artery and its branches as possi-

Figure 8.1

The upper pole is prepared and resected with ligation of the superior thyroid artery and vein

ble, because it supplies the blood to both parathyroid glands. Truncal ligation of the inferior thyroid artery should therefore be omitted, but it is sometimes helpful to hold the trunk of the artery using a vessel loop in order to facilitate further exposure of the RLN. The nerve may easily be found at a very constant landmark, the so-called tubercle of Zuckerkandl, where the RLN crosses beneath the thyroid gland and enters below the ligament of Berry into the thyroid cartilage [8].

The next step is the delivery of the thyroid gland by blunt dissection with the finger inferiorly, completed by sharp dissection under direct vision. If the gland extends to the aortic arch and thus may not be fully accessible with one's finger, a sterile soup spoon can be slipped along the anterolateral aspect of the thyroid, breaking the negative intrathoracic pressure. After elevating the gland from the mediastinum, the inferior vascular structures are ligated as near to the gland as possible. At this point, it is essential not to tear the inferior thyroid vein, as bleeding can be very brisk. Sternotomy may be needed to control these unseen vessels.

Traction on the RLN must carefully be avoided during this maneuver, and the capsule of the gland should not be opened because of possible unsuspected malignancy. If the thyroid lobe cannot be brought to a cervical position, another possibility to provide more room is to remove the opposite, smaller lobe of the thyroid from its cervical position. Hemostasis control is performed meticulously, and no drainage is used. A Cochrane review of 13 randomized controlled trials including 1646 participants did not find any clear evidence for better outcomes when drains were used [9]. The muscles are reapproximated continuously with a 3-0 absorbable suture, the platysma with a 4-0 suture, and the skin intradermally with a 5-0 absorbable suture. A smooth collar may be used for the first 24 h, and placing the patient in a 30° reverse Trendelenburg position postoperatively is advisable.

Figure 8.1

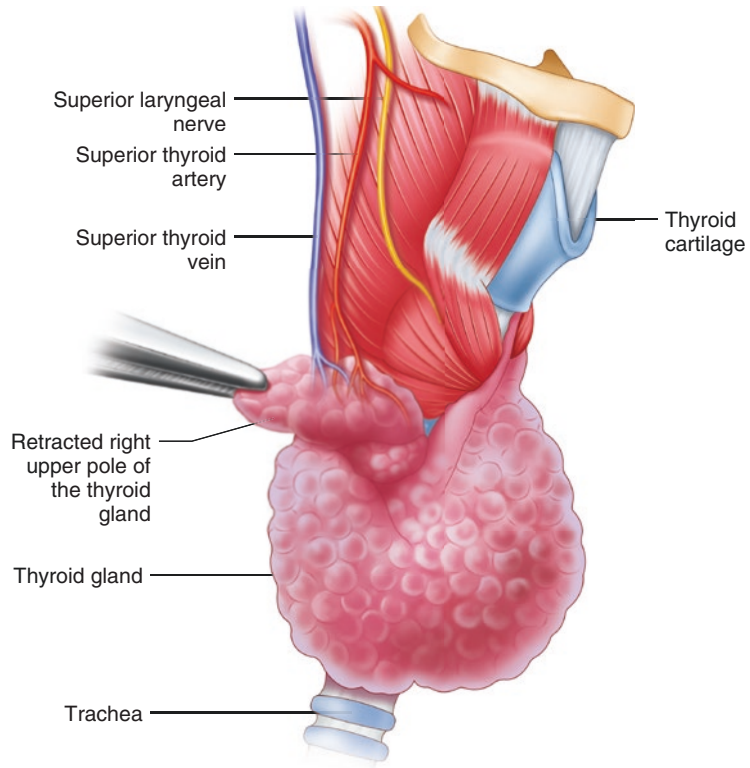
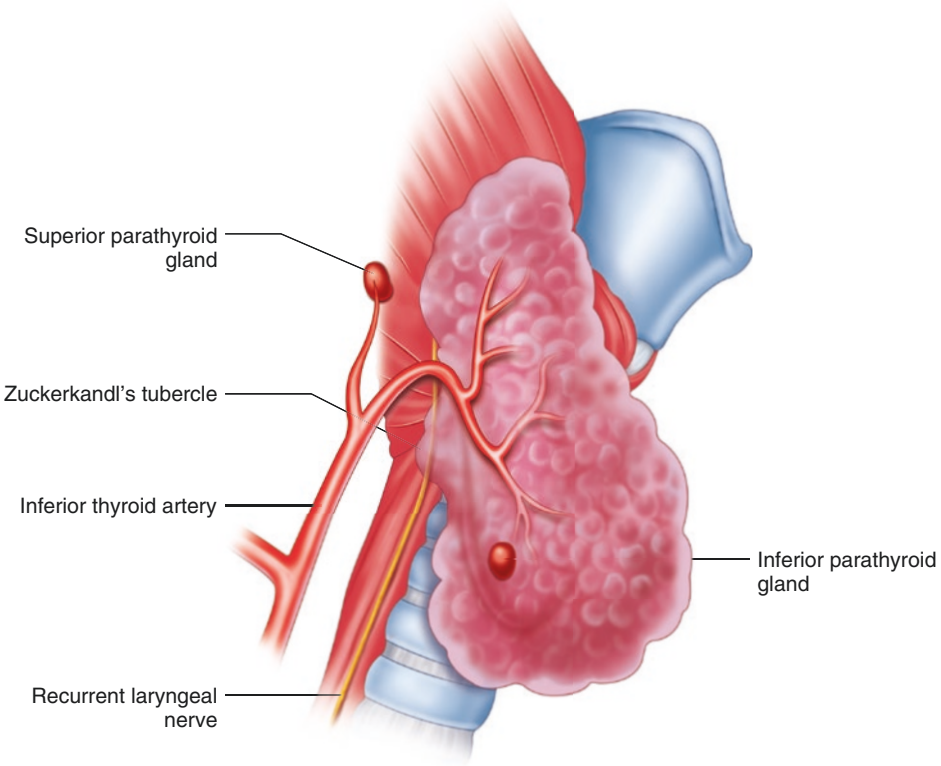


Figure 8.2

The superior parathyroid gland and the recurrent laryngeal nerve (RLN) are routinely identified

Figure 8.2


Superior parathyroid gland
Zuckerkandl's tubercle
Inferior thyroid artery
Recurrent laryngeal nerve
Inferior parathyroid gland

8.2.2 Mediastinal Extension

In cases of very large intrathoracic goiters, invasive tumors, dense adhesions from prior surgery, uncontrollable bleeding, or with the rare truly ectopic intrathoracic gland with its major blood supply from intrathoracic vessels, a mediastinal approach using sternotomy is required. As an alternative to complete sternotomy, a partial upper sternal split (i.e., manubriotomy) is sufficient in most cases to achieve adequate exposure. This means that only the manubrium is split downwards to the manubriosternal junction. Figure 8.3 depicts the skin incision for partial sternotomy (manubriotomy). After division of the subcutaneous layer, the fascia of the pectoral muscles is incised, and access to the sternal periosteum is freed.

The suprasternal notch is prepared and the innominate vein and the pleura are freed from the posterior surface of the manubrium. The manubrium is then divided using either sternal scissors (i.e., Schumacher's scissors) or a sternal saw in the midline and is gently spread with a right-angled retractor (Fig. 8.4). A pediatric thoracotomy retractor is helpful in this situation. Bleeding points from the anterior and posterior sternal periosteum and from the bone are coagulated. For better visualization, the thyroid gland is rotated forward, and the esophagotracheal groove and the angle formed by the arch of the aorta and the innominate artery are carefully prepared. The RLN is then dissected off the gland. The RLN can take unusual courses owing to the growth of large goiters, so it is wise to transect the thyroid vessels after proper identification of the RLNs. Thereafter,

Figure 8.3

The skin incision for manubriotomy (partial sternotomy)

the inferior pole vessels are divided, followed by the branches of the inferior thyroid artery, always close to the thyroid capsule. Here, the search for the lower parathyroid glands is very important. If these glands cannot be preserved at their vascular supply or doubt about their viability arises, they should be taken out, cut in small pieces, and transplanted into a formed pouch of the sternocleidomastoid muscle.

The manubriotomy or sternotomy is closed using sternal wires that are supported by strong, absorbable threads.

Large goiters with intense adhesions to the pleura or pericardium may require the excellent exposure available with a complete sternotomy. For a complete sternotomy, the skin incision is extended to just above the xiphoid process, and the pericardial and diaphragmatic attachments are freed from the back of the sternum before its division (Fig. 8.5). The following surgical dissection steps and the wound closure are similar to the description above for Fig. 8.4.

Occasionally, substernal goiters developing on the left side can cross over to the right mediastinum dorsally from the trachea, perhaps because their downward progression has been stopped by the aortic arch on the left side. For resection of this posterior mediastinal goiter, a combined approach and right anterolateral thoracotomy through the 4th or 5th intercostal space can be helpful. The patient is placed in a 45° oblique position with the right arm extended over the head (Fig. 8.6). This approach permits simultaneous cervical and thoracic exploration, and the table may be rotated from side to side to facilitate whichever part of the dissection is being performed.

Figure 8.3

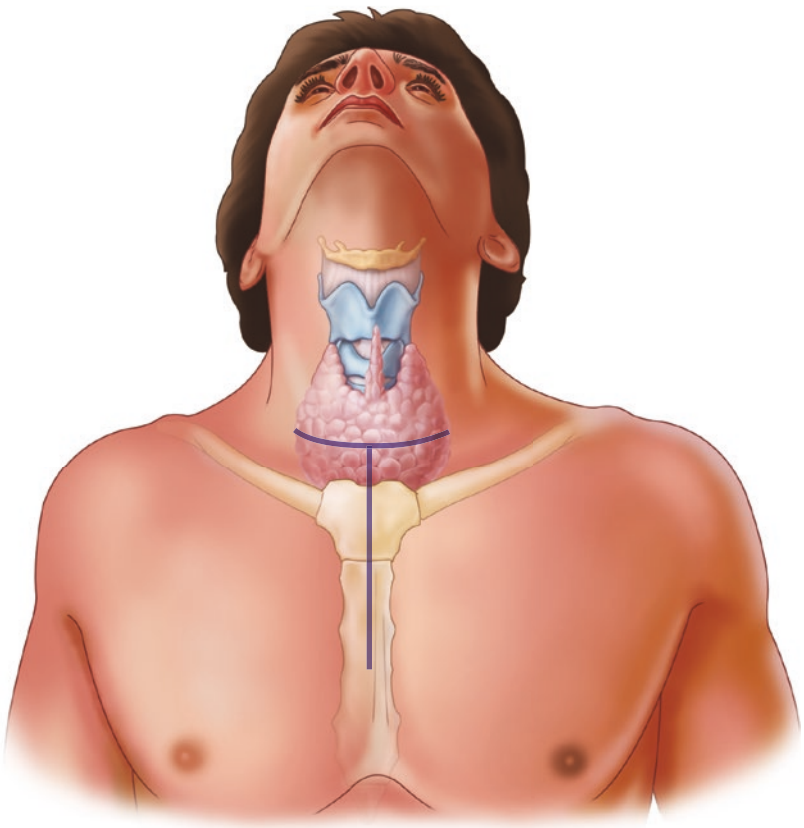


Figure 8.4

The manubrium is divided in the midline and is gently spread with a right-angled retractor

Figure 8.5

For a complete sternotomy, the skin incision is extended to just above the xiphoid process, and the pericardial and diaphragmatic attachments are freed from the back of the sternum before its division

Figure 8.4

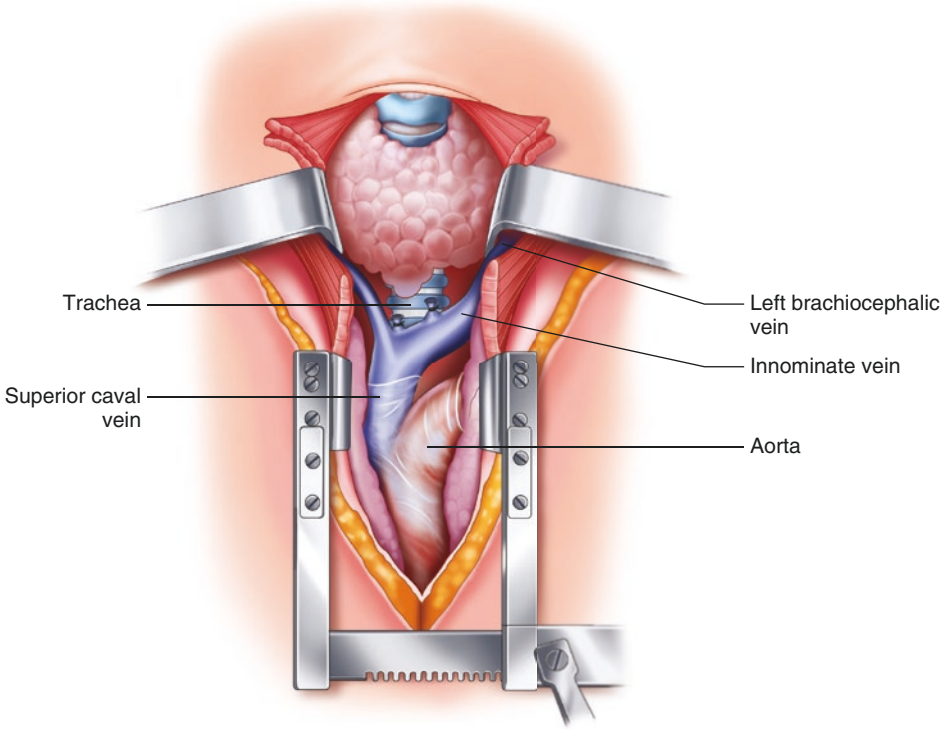


Figure 8.5

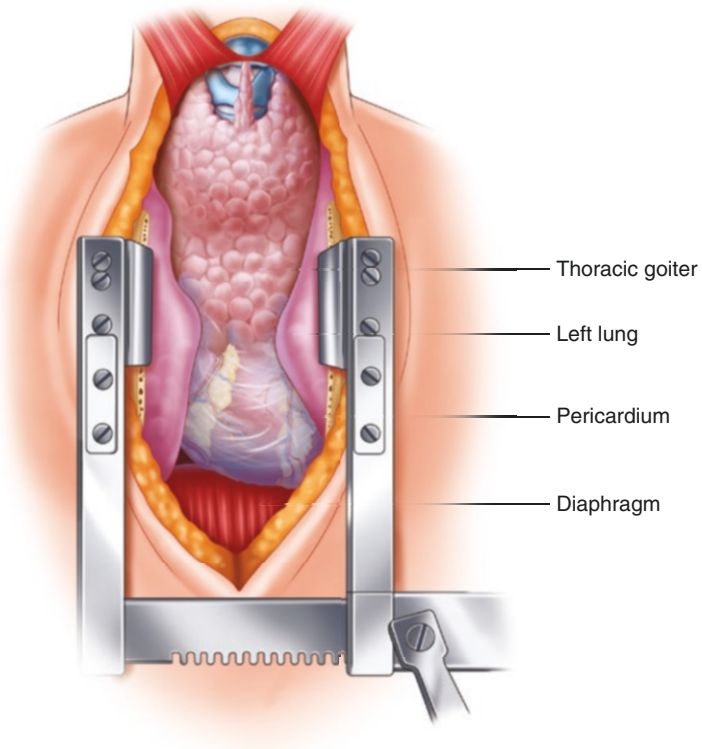
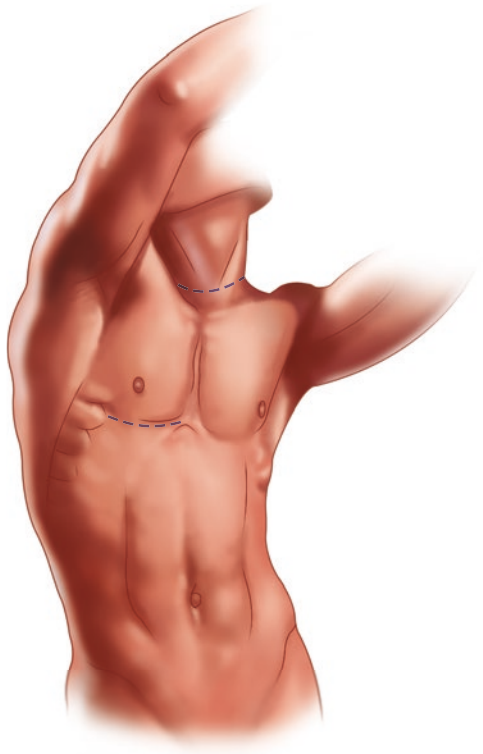


Figure 8.6

To achieve a combined approach with right anterolateral thoracotomy, the patient is placed in a 45° oblique position with the right arm extended over the head

Figure 8.6



8.3 Complications of Substernal Goiter Surgery

As with cervical goiter, the main complications of substernal goiter surgery are hemorrhage, RLN injury, and hypoparathyroidism. An intrathoracic goiter was found to be an independent risk factor for postoperative complications [10]. In a prospective study of 2235 thyroid resections, 312 were performed for substernal goiter [11]. At surgery for substernal goiter, the complication rate was significantly elevated, including secondary hemorrhage (3.2%), wound infections (2.2%), hypocalcemia for less than 6 months (24.7%), and transient RLN paresis (6.4%). The rate of persistent hypocalcemia (1.3%) or permanent RLN palsy (1.0%) was not significantly higher than in the entire patient population, however.

The surgical access also may lead to mediastinal injuries. If mediastinal hemorrhage occurs, immediate reoperation is indicated in order to avoid tracheal compression with consequent intubation problems or asphyxia. In the case of sternotomy, injury to the innominate vein may cause major hemorrhage. To gain control of the hemorrhage, the vein is compressed against the back of the sternum, the ends are identified, and the vein is sutured. Complete sternotomy is necessary in these cases. Pneumothorax after pleural injury is treated with insertion of a chest tube. More rare complications are infections, mostly due to an infected hematoma; injury of the pharynx, the trachea, or the stellate ganglion, with resultant Horner's syndrome; accessory nerve paresis; injury to the neck vessels; or tracheomalacia. Sternal infection may manifest late and is treated with a surgical débridement. Surgical mortality rates are reported to be 1% or less in these cases [3, 4].

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Modified Neck Dissection for Differentiated Thyroid Cancer

9

Iain J. Nixon and Jatin P. Shah

9.1 Introduction

Lymph node metastases occur early and often in papillary thyroid cancer, the most common differentiated cancer of the thyroid gland. Therefore, it is critical that surgeons involved in the management of patients with differentiated thyroid cancer (DTC) understand the biological progression of metastases to regional lymph nodes, and its implications, so as to perform anatomically appropriate and oncologically effective neck dissection, when indicated. Microscopic dissemination of papillary carcinoma occurs quite often: As many as 60% of patients harbor occult metastases in the clinically negative neck at the time of initial diagnosis of the primary tumor [1]. Clinically apparent or radiologically demonstrated metastases are present in no more than 10–15% of patients at initial presentation. Nevertheless, despite the large number of patients having micrometastases at initial presentation, only 4–5% of these patients progress to clinically apparent metastases, if they are observed after surgery of the primary tumor without elective regional node dissection. Their long-term survivorship and disease-specific mortality is not affected by this approach of observation of the clinically negative neck, with therapeutic neck dissection when these nodes become clinically apparent. It is also well known that the vast majority of patients—even those with nodal metastases at presentation—will be cured of disease with appropriate initial surgery, with minimal morbidity from their procedure. The surgeon who embarks on neck dissection for DTC must therefore be knowledgeable about the patterns of neck metastases from thyroid cancer and competent to resect all clinically significant disease—while identifying, protecting, and preserving all vital structures within the lateral neck.

It is important at this juncture to define the role of neck surgery for patients with DTC. Although the role of elective central-compartment neck dissection remains controversial, there is general agreement that elective lateral neck dissection is not indicated in those patients who have no evidence of metastases in the lateral neck on clinical examination or imaging. Up to 25% of patients with DTC who are considered cN0 can be shown to have pathologically demonstrable thyroid cancer cells (occult metastases) in elective neck dissection specimens [1], but the impact of these occult metastases on clinical outcome is minimal, if any. Only a minority of these patients progress to develop clinically significant disease during follow-up. Those who do manifest clinical disease during follow-up can be adequately treated with a therapeutic neck dissection, without adverse impact on prognosis. Further, about 10% of patients undergoing elective neck surgery suffer significant morbidity, including increased incision length and anesthesia/paresthesia of the skin in the cervical region. For all these reasons, elective lateral neck dissection is not recommended [2].

The patterns of neck metastases from DTC are well known. The first-echelon lymph nodes are located in the central compartment of the neck at level VI. These include lymph nodes in the prelaryngeal region as well as Delphian nodes and perithyroid, pretracheal, paratracheal, and paraesophageal nodes up to the suprasternal notch. Further progression of nodal spread occurs to lymph nodes at levels VII and IV. In these patients, dissemination to deep jugular nodes at levels II, III, and V is common (Fig. 9.1). Bilateral involvement is quite common. In those patients with preoperative evidence of nodal disease, surgery should eradicate all gross disease, but also encompass each level considered to be at high risk of harboring occult metastases. Rates of metastasis are highest to levels IIa to Vb, with disease less common at levels I, IIb, and Va (Fig. 9.2). For most patients, the operation of choice is thus a selective neck dissection with resection of the lymphatic

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J.R. Howe (ed.), *Endocrine and Neuroendocrine Surgery*, Springer Surgery Atlas Series, DOI 10.1007/978-3-662-54067-1_9

structures from levels IIa, III, IV, and V [3]. This procedure will often be performed with a total thyroidectomy and central compartment node dissection, although in the setting of recurrent disease in the lateral neck, it may be performed without exposure of the central compartment.

If there is preoperative evidence of disease within levels I, IIb, or V, these levels should also be encompassed during neck dissection. The presence of bulky nodal metastases in adjacent levels is also an indication for comprehensive level I–V neck dissection. In order to comprehensively excise all

Figure 9.1

Levels of the central (**a**) and lateral (**b**) neck

Figure 9.2

Rates of metastasis are highest to levels IIa to Vb, with disease less common at levels I, IIb, and Va

involved nodal regions, a contrast-enhanced CT scan of the neck and mediastinum is recommended for accurate assessment of the anatomic extent of nodal metastases. This may delay the administration of postoperative radioactive iodine (RAI) by a few weeks, but it will ensure completeness of nodal clearance, and thus significantly reduce the incidence of missed metastatic nodes, a common cause of recurrent nodal metastases in the neck.

Figure 9.1

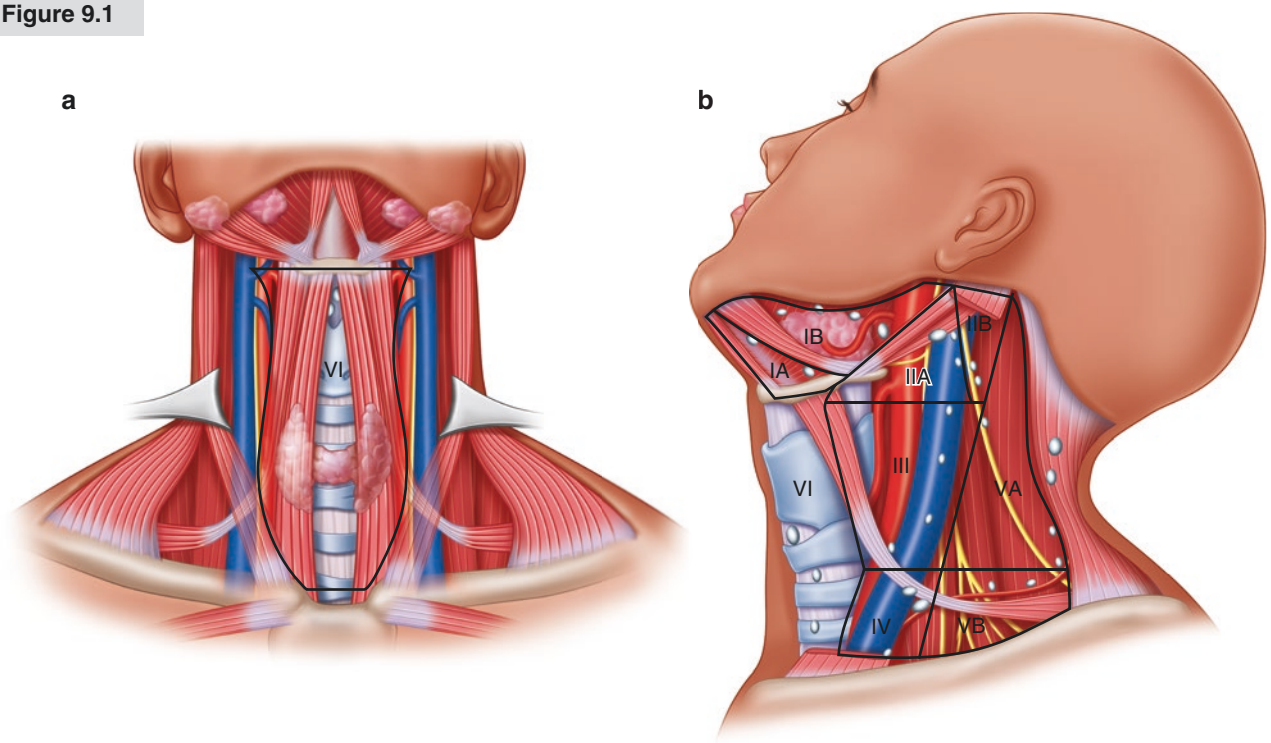
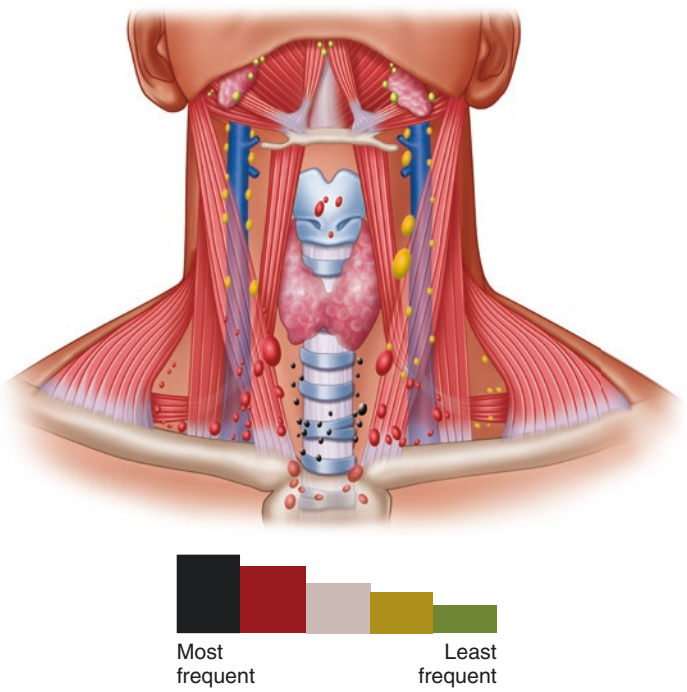


Figure 9.2



9.2 Modified Neck Dissection for Lateral Cervical Lymphadenectomy

9.2.1 Incision Planning

When considering an incision, the surgeon must ensure that adequate access will be available to all levels of the neck planned for excision. Previous incisions, as well as the potential need for further surgery on the ipsilateral lateral, central, and contralateral neck, also should be considered in planning the incision.

Traditional J-shaped incisions, which ran from the mastoid process, curving down into the neck and joining the thyroidectomy incision, crossed the lines of relaxed skin tension and therefore resulted in poor cosmetic outcomes. Instead of that incision, we recommend a single transverse incision at about the level of the cricoid cartilage, extended on either side as necessary to provide all the necessary exposure for thyroidectomy and appropriate regional node dissection as needed (Fig. 9.3). A well-placed incision, usually in a skin crease slightly above the level of the cricoid cartilage, can be extended to both sides of the neck, affording access to all levels of the neck and leading to optimal cosmetic outcome without compromising surgical access [4]. If there is a scar from a previous thyroidectomy incision, then every attempt should be made to incorporate that scar in the neck dissection incision, if possible. Doing so will avoid multiple scars and minimize potential vascular compromise of the skin island between old and new incisions.

When performing a neck dissection from levels IIa to Vb, the incision should extend to the lateral border of the sternocleidomastoid muscle, and far enough across the midline to allow retraction to expose the accessory nerve in level II.

For access to perform unilateral or bilateral comprehensive modified neck dissections of levels I through V, this incision can be extended from the anterior border of the ipsilateral trapezius muscle to the contralateral trapezius if required to encompass levels Va, IIb, and I.

9.2.2 Raising Skin Flaps

The skin incision is made using a scalpel, and the platysmal layer is identified deep to the superficial fat. Subsequent dissection proceeds with the use of electrocautery, set at an appropriate level to maximize hemostasis and minimize charring of tissue. The platysma is incised throughout the length of the incision. At the lateral margins of the incision, and in the midline region, the platysma is flimsy or absent. By dissecting on a broad front, with adequate retraction of the skin edge using sharp hooks, the surgeon can easily identify a subcutaneous plane corresponding to the undersurface

Figure 9.3

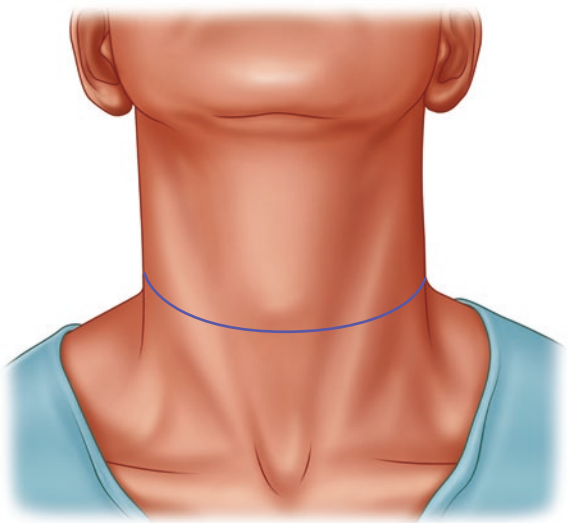
A single transverse incision at about the level of the cricoid cartilage, extended on either side as necessary, can provide all the necessary exposure for thyroidectomy and appropriate regional node dissection with optimal cosmetic outcome

of the platysma, which allows the flaps to be elevated with minimal blood loss.

Particular attention should be paid to the marginal mandibular branch of the facial nerve during elevation of the upper flap. This structure lies deep to platysma, but superficial to the fascial capsule of the submandibular gland. As the upper skin flap is elevated, the contour of the lower border of the submandibular salivary gland can be identified just cephalad to the digastric muscle. At this point, if level I is not to be dissected, then no further superomedial elevation of the flap is required, and the inferior surface of the submandibular gland can be mobilized superiorly to expose the digastric muscle, marking the superomedial limit of dissection. This landmark is vital to the procedure and should be dissected free from the hyoid to the mastoid process. To expose the digastric muscle completely, the common facial vein and other venous tributaries crossing the digastric muscle from the superficial surface of the submandibular gland should be divided and ligated. If level I is to be included, however, dissection proceeds under the glandular fascia, which is then elevated off the gland in a superior direction, with the marginal mandibular nerve contained within the fascial tissue superficial to the gland. This dissection is continued up over the mandible, thereby dissecting, shifting, and retracting the nerve out of the field of dissection to safety. The upper skin flap should be carefully elevated over the surface of the sternocleidomastoid muscle, so as to protect and preserve the greater auricular nerve and to minimize skin anesthesia/paresthesia following surgery.

The inferior skin flap should be elevated in a similar fashion down to the level of the clavicle. Because all nodal dissection is done in a plane deep to the sternomastoid muscle, it is not necessary to raise the skin flaps over the posterior triangle lateral to the posterior border of the sternomastoid muscle. Avoiding this step during elevation of the flaps protects the accessory nerve in the posterior triangle, preventing any inadvertent injury to it. Elevation of the skin flap over the posterior triangle is required only if there are grossly enlarged metastatic nodes in the posterior triangle of the neck. In that setting, extreme care must be exercised to find the accessory nerve at Erb's point, where it exits from the sternomastoid muscle and runs inferolaterally to enter the trapezius muscle. The cranial branch of the accessory nerve is joined by a spinal contribution from the cervical plexus at the root of C2, and care should be taken to preserve both branches in an attempt to minimize shoulder dysfunction. If level V is to be formally dissected, exposure of the trapezius muscle superiorly allows dissection to proceed on its lateral aspect. The accessory nerve enters the muscle on its medial surface, so using this technique protects the nerve.

Figure 9.3



9.2.3 Selective Neck Dissection of Levels IIa, III, IV, and Vb

At this stage, the borders of the dissection field are exposed. The deep cervical fascia at the anterior border of the sternomastoid muscle is divided, and dissection proceeds along the medial aspect of the muscle, to allow its retraction laterally. Small blood vessels entering the muscle are divided and ligated. These can be expeditiously controlled with the use of either electrocautery or hemostatic devices such as LigaSure™ (Covidien, Mansfield, MA) or harmonic scalpel. The plane is followed posteromedially until the roots of the cervical plexus are identified. These structures mark the level of the base of the dissection. Several hemostats are then applied to the nodal tissue in the deep jugular chain, allowing its traction medially and thus permitting retraction of the specimen medially to facilitate dissection of lymph nodes lateral to the internal jugular vein and overlying the roots of the cervical plexus. Deep right-angled retractors or small Richardson retractors are used to retract the sternomastoid muscle laterally. With adequate retraction, a plane between the floor of the posterior triangle and the specimen is defined from the level of the accessory nerve superolaterally to the level of the clavicle inferiorly.

Having identified the superficial, deep, posterior, and superior borders of the dissection, the specimen is now dissected in a lateral-to-medial and either superior-to-inferior or inferior-to-superior direction, depending on the extent and level of gross disease. Usually, the most significant disease is addressed as the final part of the dissection, in order to maximize access to the most challenging part of the dissection. It is generally preferable to dissect from the superior aspect in an inferior direction, following the accessory nerve as it passes under the digastric to run lateral to the internal jugular vein. Retraction of the digastric muscle exposes the carotid sheath, and careful dissection allows identification of the internal jugular vein. Small venous tributaries overlying the surface of the internal jugular vein must be divided and electrocoagulated or ligated. In some patients, the occipital artery crosses the internal jugular vein on its surface and requires division and ligation. This landmark is crucial, and great care must be taken not to injure the great vessels as they pass into the skull base.

The fascia of the vein is dissected to identify a clean plane separating the vein from the specimen, which is mobilized, forming the superior corner of the dissection. Meticulous attention is paid to clearing the jugulodigastric lymph nodes at level IIa. Doing so will expose the accessory nerve laterally. Dissection of level IIb is not necessary unless gross metastatic lymph nodes are present at level IIa. The specimen can gently be dissected free of the internal jugular vein in an inferior direction. Dissection proceeds down the length of the jugular vein, remaining superficial to the branches of the cervical plexus and the prevertebral fascia, in order to protect the phrenic nerve. The full length of the carotid sheath will gradually be exposed.

The lateral aspect of the specimen is thus mobilized, elevating it from the plane of the cervical plexus, allowing the specimen to be elevated from the floor of the neck. The omohyoid muscle is divided to allow mobilization of structures from level IV. As dissection continues in this area, the transverse cervical vessels will be identified, and the superior branch of the artery should be isolated and divided, acting as a convenient marker of the most inferior extent of the dissection, assuming that there is no palpable disease deep to these structures.

The nodes that lie posterior to the carotid sheath, separating levels IV and VI, are a common site of metastasis from

Figure 9.4

The nodes that lie posterior to the carotid sheath, separating levels IV and VI, are a common site of metastasis from thyroid cancer

thyroid cancer. Particular attention should be paid to identifying and excising any pathological tissue here, as this is a common site of regional failure (Fig. 9.4).

At this point, the plane of dissection will be clearly evident. Dissection continues to free the vein from the specimen, being vigilant to identify the vagus nerve throughout its length. As the specimen is rotated anteromedially, small venous tributaries to the internal jugular vein are exposed and should be carefully divided to free the specimen from the vein.

The most inferior and lateral aspect of the jugular vein requires special attention. On both sides of the neck, prominent lymphatic channels pass in a leash up into the neck from the thoracic (or accessory thoracic) duct. If these structures are divided without prior ligation, a chyle leak will result. Instead, the lymphatic structures should be carefully isolated, clamped, and divided, with ties placed to prevent this significant complication. Once the dissection of the lymph nodes in the posterior triangle lateral to the internal jugular vein is completed, attention is focused back to the upper part of the neck, where dissection proceeds over the jugular vein. Medial to the internal jugular vein and over the lateral aspect of the carotid artery, the hypoglossal nerve is identified. Often the descendens hypoglossi branch can be traced superiorly to identify the nerve, which is tethered inferiorly by the occipital branch of the external carotid. Dissection continues medially and inferiorly to the digastric muscle, protecting the hypoglossal nerve throughout its course until it turns superomedially under the mylohyoid muscle. Several pharyngeal veins must be divided to free up the specimen. These are carefully ligated. At this juncture, the common facial vein will be seen entering the internal jugular vein. It is clamped, divided, and ligated (Fig. 9.5).

Having mobilized the specimen off the jugular vein at the upper end, the omohyoid muscle should now be followed superomedially. It is detached from the hyoid bone. The specimen is now attached through soft tissues at the carotid bulb and the superior thyroid artery. The superior thyroid vessels are preserved by careful gentle dissection, but a branch of the superior thyroid artery coming off its superior surface will need to be divided and ligated. Extreme care should be exercised at this level to avoid injuring the superior laryngeal nerve. The remaining soft tissues are divided, and the specimen is delivered (Fig. 9.6). Because the specimen contains no anatomic structures other than lymph nodes and fat, it should be marked with tags to identify levels of lymph nodes, or it may be divided to separate out each level, to allow a level-specific pathological analysis.

The wound should be inspected for complete hemostasis and irrigated. Any sites of hemorrhage should be controlled with the use of diathermy and ties. At this point, it is often advisable to place the patient head-down or to perform a Valsalva maneuver in order to identify any additional bleeding points, and more importantly, to check for a chyle leak. After ensuring a dry field, a suction drain should be placed under the sternomastoid muscle to apply negative pressure to the skin flaps. The drain is inserted through a separate incision in the postauricular region, and placed deep to the sternomastoid muscle down to the supraclavicular region. The drain should remain on wall suction (high negative pressure) for 24–48 hr to allow the skin flaps to adhere to the deep tissues of the neck, thus minimizing the risk of seroma or hematoma. The wound is closed in layers, with interrupted absorbable sutures for the platysmal layer and interrupted nylon for the skin (Fig. 9.7).

Figure 9.4

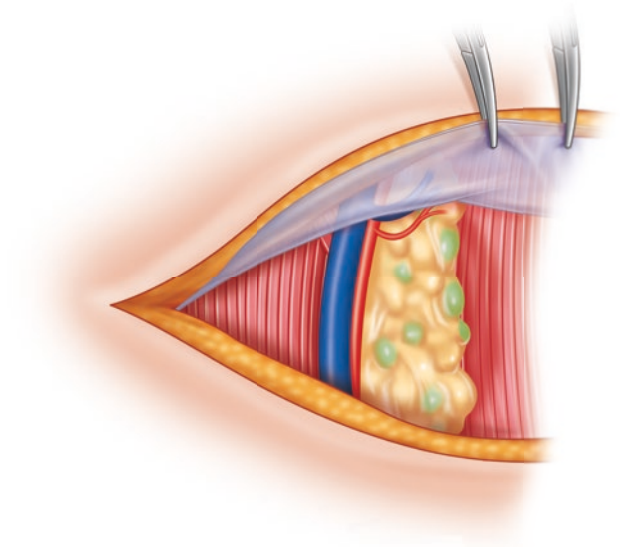


Figure 9.5

The common facial vein is clamped, divided, and ligated before it enters the internal jugular vein

Figure 9.6

The remaining soft tissues are divided, and the specimen is delivered. It should be marked to identify levels of lymph nodes, or it may be divided to separate the levels

Figure 9.5

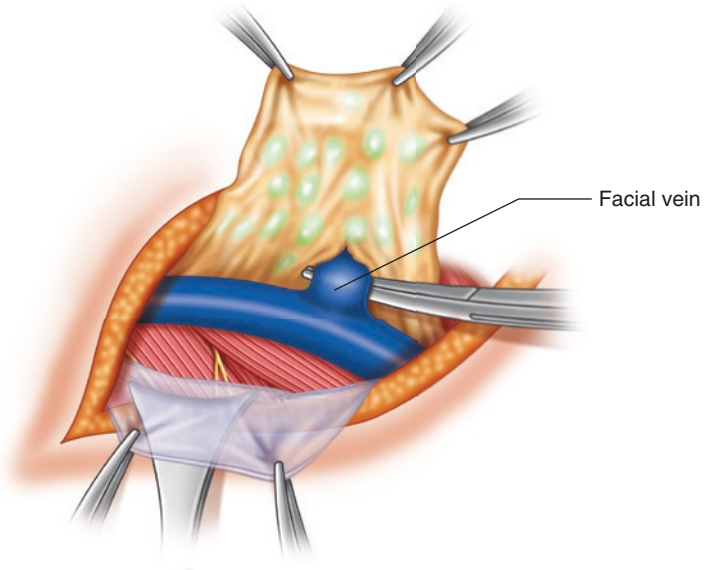


Figure 9.6

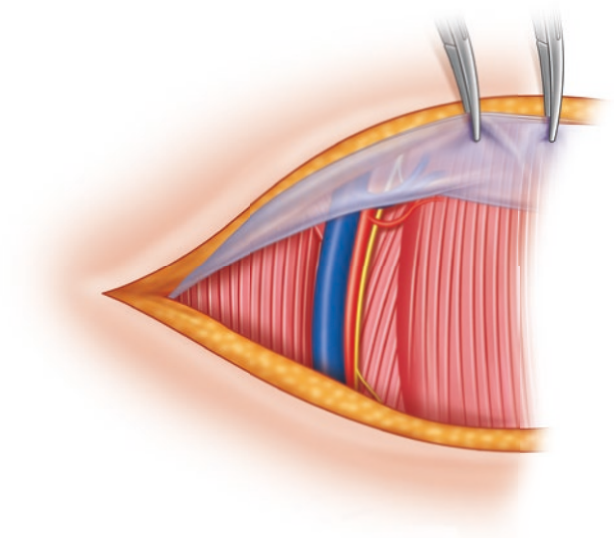
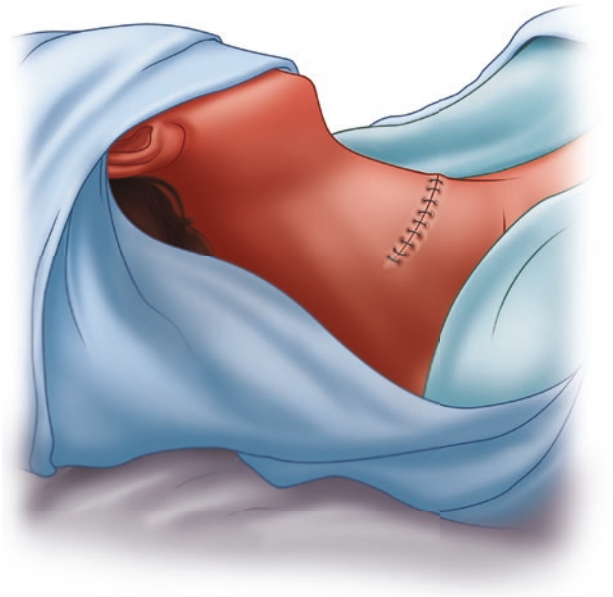


Figure 9.7

The wound is closed in layers, with interrupted absorbable sutures for the platysmal layer and interrupted nylon for the skin

Figure 9.7



9.2.4 Comprehensive Neck Dissection of Levels I Through V

In the presence of bulky, multilevel nodal metastases, a comprehensive modified neck dissection should be performed, encompassing all five levels in the lateral neck. It is extremely rare for DTC to present with gross extranodal extension requiring sacrifice of the sternomastoid muscle, accessory nerve, and jugular vein. Thus a true radical neck dissection is rarely indicated. On the other hand, it is not uncommon to have invasion of the internal jugular vein by bulky metastases, requiring its sacrifice. Extension of the procedure described above is required to achieve selective clearance of levels I, IIb, and V. The skin incision should be extended to the level of the trapezius muscle. The superior flap should be elevated to expose the inferior border of the mandible, still preserving the marginal mandibular nerve. The accessory nerve should be identified and traced both superiorly, under the digastric muscle, and inferiorly, in the floor of the posterior triangle lateral to the sternomastoid muscle, preserving both the cranial and spinal components.

Retraction of the sternomastoid muscle allows access to level IIb. By placing right-angled retractors under the sternomastoid muscle and over the digastric muscles, the lymphovascular tissue around the upper end of the accessory nerve can be exposed and dissected from the floor of the neck. The specimen is dissected from the deep neck muscles inferomedially toward the accessory nerve. Mobilization of the specimen from the lateral aspect of the jugular vein is also required at this point. The nerve should be freed from the underlying tissue in order to allow the specimen to be passed under the nerve while preserving its continuity. The nerve at this level is thus circumferentially dissected, to mobilize the specimen of level IIb nodes. These nodes remain attached to level II nodes, and the dissection then proceeds as described above.

With the lateral border of the trapezius on display, tissue superior to the accessory nerve can be dissected free from the prevertebral fascia in a medial direction. Again the nerve is freed from the underlying tissue to allow delivery of level Va and mobilization of level Vb. The specimen from the posterior triangle is thus dissected off from the trapezius and off from the splenius capitis and levator scapulae, medially towards the sternomastoid muscle, identifying the roots of

Figure 9.8

The specimen from the posterior triangle is dissected off from the trapezius, the splenius capitis, and the levator scapulae, medially towards the sternomastoid muscle. The roots of the cervical plexus are identified and the specimen is dissected off from them

the cervical plexus and dissecting the specimen off from them as described above (Fig. 9.8).

The specimen mobilized from behind the sternomastoid muscle should be freed from the muscle by incising the fascia surrounding the muscle at its lateral border and retracting the muscle medially from the tissues below. This allows the specimen to be delivered under the muscle to complete the dissection from the carotid sheath. Having dissected levels II through V, the specimen remains on a pedicle to level I. The submandibular gland should be identified and dissected from its fascial connections to the inferior border of the mandible. The facial vessels are identified; it is crucial to remember that the marginal mandibular nerve runs immediately superficial to the facial vein. The vein may be divided and reflected superiorly in order to protect the nerve. The facial artery passes from deep to the digastric up through the submandibular gland and over the mandible, so it is often encountered twice during the dissection and should be controlled with care.

With the submandibular gland mobilized, the mylohyoid muscle is identified and separated from the gland. Multiple thin-walled vessels to the mylohyoid muscle are often encountered during this approach to the floor of mouth; they should be carefully controlled to prevent venous bleeders, which will retract behind the mandible. A retractor is inserted under the mylohyoid muscle, allowing exposure of the lingual nerve and the secretomotor fibers to the submandibular gland. The lingual and hypoglossal nerves should be identified prior to division of any structures at this point. The lingual nerve can be seen to pass down towards the gland, tethered by the submandibular ganglion. A small artery that runs with the ganglion should be divided and tied, allowing the lingual nerve to retract superiorly out of the field of dissection. The hypoglossal nerve may be traced from its position in level II, or identified in a plane deep to the level of dissection. Ligation of the submandibular duct (Wharton's duct) allows the gland to be mobilized completely (Fig. 9.9).

The remaining level I dissection proceeds along the inferior border of the mandible. Tissues should be elevated from the underlying anterior belly of the digastric muscle up to the midline. The specimen is then dissected, following the muscular plane back to the level of the hyoid, and is delivered en bloc.

Figure 9.8

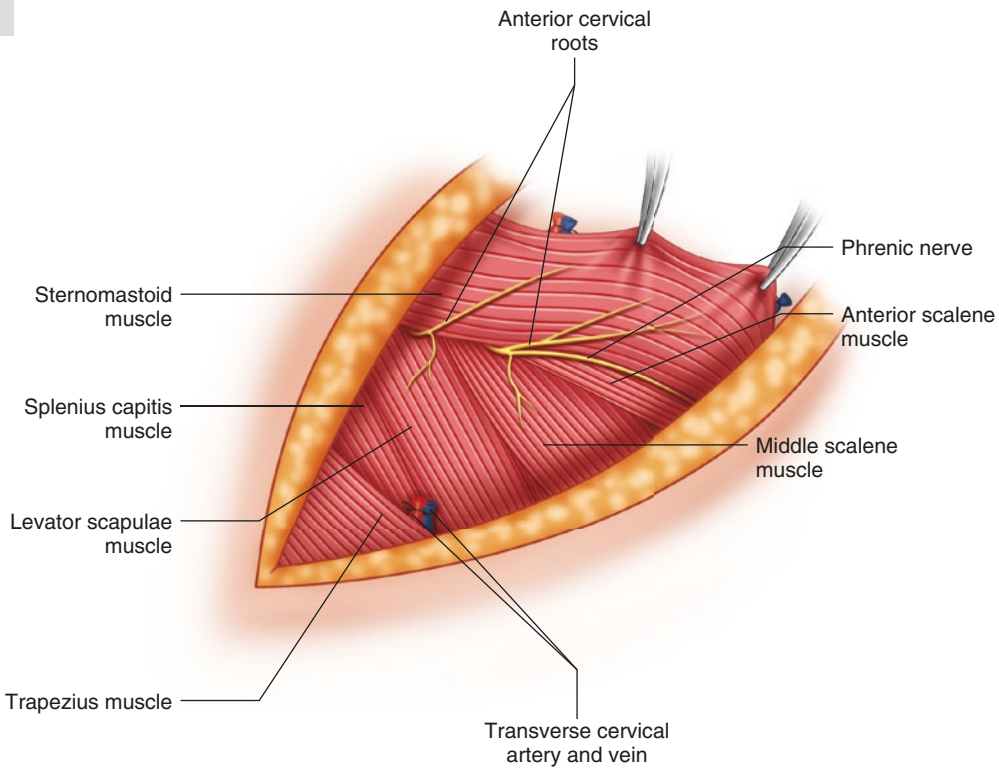
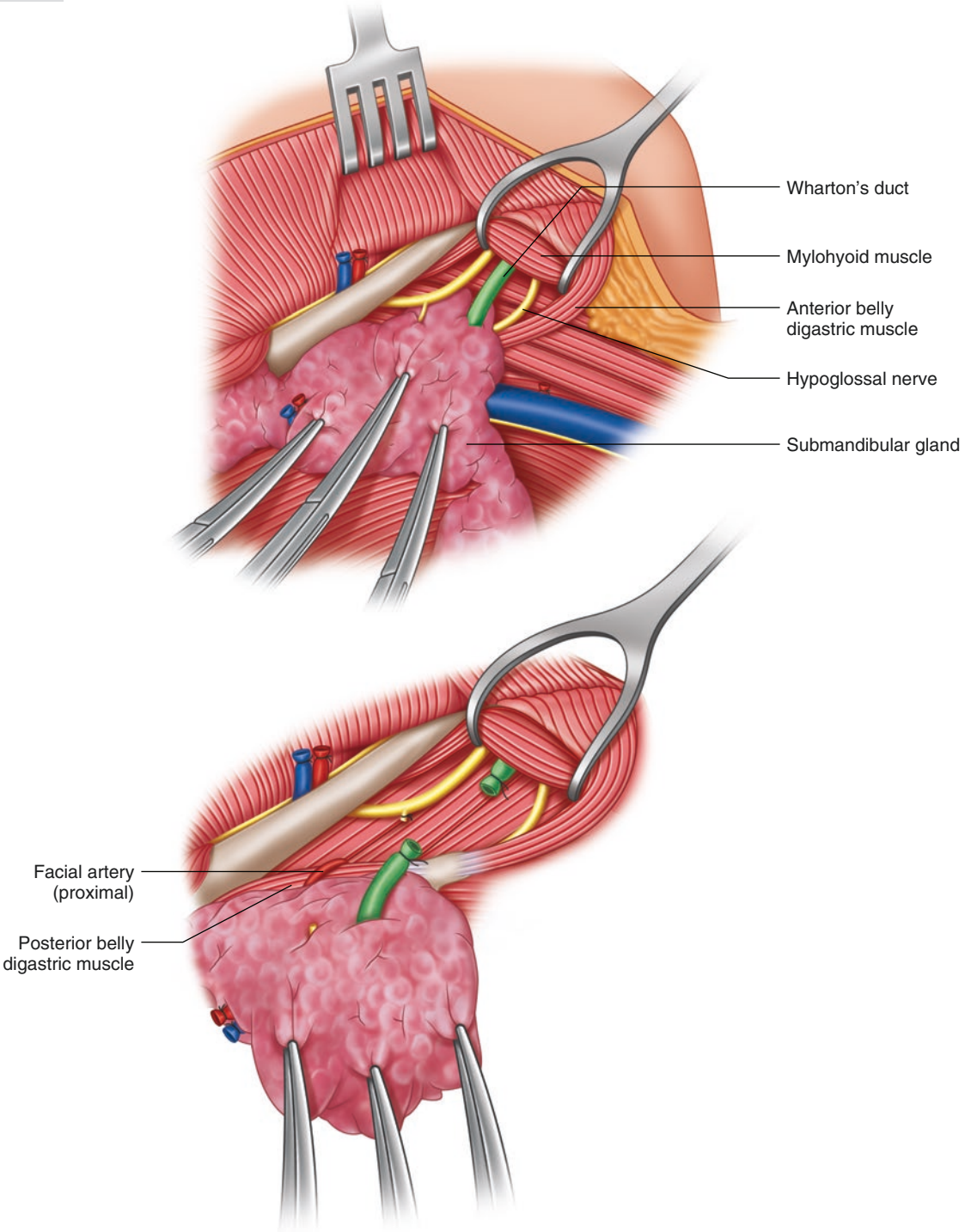


Figure 9.9

Ligation of the submandibular duct (Wharton's duct) allows the submandibular gland to be mobilized completely

Figure 9.9


Wharton's duct
Mylohyoid muscle
Anterior belly digastric muscle
Hypoglossal nerve
Submandibular gland
Facial artery (proximal)
Posterior belly digastric muscle

9.3 Discussion

The presence of clinically apparent nodal metastases in the lateral compartment of the neck predicts the risk of future recurrence in all patients and of disease-specific death in older patients [2, 5]. Treatment should aim to eradicate gross disease and encompass all high-risk areas for metastasis while minimizing the morbidity of surgery. Patients with DTC are very unlikely to die of their disease; many live for decades after diagnosis, and although it is important to rid patients of overt nodal disease, there is no clinical benefit in identifying occult or microscopic disease by elective neck dissection. Instead, clinicians should focus on minimizing the morbidity of treatment. It is not worth damaging the marginal mandibular or spinal accessory nerve in order to remove microscopic occult disease that is unlikely ever to develop into clinically significant disease.

In the presence of overt nodal disease, however, every attempt should be made to comprehensively dissect all at-risk levels. Incomplete clearance of all nodal regions at risk almost always results in recurrence. Accurate preoperative imaging therefore is crucial to a comprehensive and complete clearance of regional lymph nodes. Patients with thyroid cancer expect to have excellent cosmetic, functional, and oncological outcomes. It is vital that no nodal tissue is left within the dissection bed, as salvage surgery is challenging, time-consuming, and associated with a high risk of postoperative complications. In addition to the oncological aspects of lateral neck surgery, surgeons performing modified neck dissection for thyroid cancer should be familiar with the potentially variable anatomy encountered in order to preserve the critical neurovascular structures involved. It is also important for surgeons to appreciate that with appropriate preoperative planning, a transverse incision can be placed in an appropriate skin crease, minimizing scar-related morbidity (Fig. 9.3).

When careful dissection is coupled with a thorough understanding of the patterns of lymph node metastasis, patients with lymph node metastasis can expect 10-year regional recurrence–free survival of about 95% [6]. Suboptimal surgery, with failure to comprehensively dissect all at-risk lymph node groups, however, will result in high rates of regional "in-field" recurrence, repeated surgeries, and the potential for significant iatrogenic morbidity.

9.4 Conclusions

Clinically apparent neck metastases in patients with thyroid cancer tend to present without invasion of the major structures in the neck. Nearly all of these patients will be cured with a single "complete" surgical procedure, and their life expectancy will not be shortened by their disease. By understanding the patterns of metastasis, the anatomy of the neck, and the techniques required to safely resect all gross disease and adjacent lymph node groups at risk, surgeons can maximize oncological outcomes and minimize morbidity for patients who require modified neck dissection for differentiated thyroid cancer.

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Part III

Adrenal

Open Transabdominal Adrenalectomy for Malignant Neoplasms

10

Murray F. Brennan

10.1 Introduction

Open adrenalectomy has become an uncommon operation. Minimal-access surgery has markedly improved perioperative morbidity of simple adrenalectomy, with decreased pain and a shorter hospital stay. Long-term results are equivalent in terms of outcome, so the minimal access route is to be preferred. The diminution in incisional hernia, when done by the posterior dorsal, lateral, or transabdominal open approach, is of itself sufficient to justify the minimal access approach.

Unfortunately, such minimal access approaches are neither possible nor appropriate for established malignant adrenal cortical neoplasms. The classic presentation of malignant tumors, with fever, anemia, and weight loss, is now much less common, presumably because of earlier diagnosis. Occasionally, however, it is not easy to determine whether a lesion is benign or malignant [1]. Malignant adrenal tumors are usually large, with a median size of 14 cm [2, 3]. They often involve periadrenal lymph nodes and require lymph node dissection [4]. Feminization in a male or masculinization in a female should raise a high suspicion for malignancy, even in patients with relatively small tumors. Adherence to the kidney, if not involvement, is possible but uncommon. More challenging is the intravascular growth of such lesions, typically growing in the adrenal vein, either into the vena cava directly on the right or into the left renal vein and then the vena cava on the left. Appropriate open access then becomes mandatory for the safe performance of the procedure.

Primary resection of adjacent organs must be anticipated: on the left, usually the spleen and distal pancreas, for access or invasion, and the kidney, because of lymph node or venous involvement. On the right, the kidney, liver, or vena cava are at risk.

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Reoperative adrenal surgery for recurrence or persistence is a serious and most challenging problem [5]. At the time of reoperation, simple tissue planes are often lost, and though primary resection of the liver is uncommon, it may become necessary either because of invasion or because of the difficulty of mobilization in the presence of retrohepatic adherence. Rather than anatomical resection of the liver following hepatic inflow and outflow control, it is sometimes safer to revert to the more historic anterior transhepatic approach. At the time of recurrence, resection of adjacent organs is the norm and should be anticipated.

10.2 Surgical Technique

Multiple incisions are available for appropriate access for major adrenal excision. For simple or bilateral tumors, either a long midline incision or a bilateral or unilateral subcostal incision is preferred (Fig. 10.1a). Body habitus with a wide or narrow subcostal space can influence the approach. Our preferred approach is the unilateral subcostal approach, with extension to bilateral as needed, or extension of the unilateral subcostal incision up the midline to the xiphisternum. For extended resections in which mobilization of the liver will be important, a long lumbar incision or thoraco-abdominal incision is preferred on the right side (Fig. 10.1b). These approaches can also be used on the left side, especially if diaphragmatic adherence or invasion is suspected. On the left side, access to a left adrenal tumor can commence with a left subcostal incision with ready extension into the left chest if the lesion is large or access proves difficult (Fig. 10.1c).

Access to the right adrenal is illustrated (Fig. 10.2), where the transverse colon is reflected inferiorly, the duodenum is reflected to the patient's left, and the vena cava is clearly exposed. Although the right adrenal vein is shown to be accessible in the figure, it is often posterior and the tumor extends over the vena cava, so that access to the vein is at the end of the procedure rather than at the beginning. Textbooks commonly suggest that in functional tumors the

J.R. Howe (ed.), *Endocrine and Neuroendocrine Surgery*, Springer Surgery Atlas Series, DOI 10.1007/978-3-662-54067-1_10

adrenal vein should be ligated early in the procedure, but it is rarely possible to do so with large malignant tumors. Multiple parasitic arteries exist with concomitant adrenal venous tributaries. The vena cava is exposed directly from the anterior surface, and the renal vein is identified and dissected free. Important consideration must be given to the invariably present right accessory adrenal vein draining into the right renal vein. With large tumors, this can be a large vessel that can be a source of considerable hemorrhage if it is not carefully isolated, ligated, and divided. As opposed to benign adenomas, the periadrenal vessels draining into a phrenic venous plexus or directly to the liver are also a potential source of hemorrhage and require direct visual control.

Elevation of the right lobe of the liver, with extensive mobilization if necessary, is important to gain access to the superior pole of a right adrenal tumor. Small hepatic venous tributaries draining into the vena cava are individually ligated and divided to allow safe mobilization of the right lobe of the liver. The right kidney is not electively sacrificed unless necessary for nodal dissection or (rarely) invasion. If it is clear that the kidney must be sacrificed because of superior pole invasion or to allow adequate lymph node dissection, then rotation of the kidney from the posterior aspect is helpful. With this maneuver, the posteriorly placed right renal artery can be ligated in continuity, allowing much safer and better controlled renal vein division.

The approach to the left adrenal vein often requires complete mobilization of the spleen and pancreas to gain adequate access (Fig. 10.3). Primary venous drainage on the left side is into the left renal vein. This vein often can be engorged and may contain tumor extending into it, often stopping as the vein travels in front of or behind the aorta. With large tumors, mobilization of the spleen and pancreas completely to the patient's right gives clear access to the tumor and the renal hilum. Small arterial branches from the phrenic vessels and the lateral side of the aorta must be individually ligated. With very large tumors, these vessels can be included with dissection of the soft tissues from the aorta with hemostatic clips. With all large malignant tumors, one should assume that parasitized vessels can occur on all surfaces of the tumor, and blunt dissection, as performed for small benign tumors, should not be attempted. On occasion, a hemostatic device such as a LigaSure™ (Covidien; Mansfield, MA) can be used in the posterior fat, but it is preferable to skeletonize the diaphragm under direct vision.

When tumor extends into the left renal vein through the adrenal vein, it is sometimes possible to preserve the left kidney if the left gonadal vein is not occluded or obstructed, by dividing the left renal vein just to the right of the left gonadal vein with a vascular stapler. The aorta is formally skeletonized. If pancreas invasion is expected or encountered, then the splenic artery is identified at its origin, ligated in continuity, and subsequently divided. All short gastric vessels are divided. With the splenic artery ligated, the portal vein can be dissected from above and below and the splenoportal junction can be clearly identified, isolated, and divided, either prior to or following pancreatic division.

The lymphatic drainage of the adrenal is illustrated for both the right and left side (Fig. 10.4). On the right side, the primary lymph node drainage areas are to the perinephric and renal vein sites, with small nodes extending to the hepatic vessels on both sides. Nodal disease can extend to the base of the common hepatic and splenic vessels and the celiac trunk. Although the value of extended node dissection is unproven, nodal metastases are common. Nodal dissection should be performed in continuity where possible and can proceed from medial to lateral, commencing on the right side at the base of the hepatic artery across the anterior vena cava, and extending posterior to the inferior vena cava and inferiorly to the renal vein. The renal artery can be

skeletonized superiorly. On the left side, the dissection continues along the left side of the aorta. The arterial supply to the left adrenal is often not a single vessel, but rather multiple, small arterial branches, which also occur from the phrenic artery superiorly.

The major challenge for open adrenalectomy for malignant tumor is vena cava involvement. Usually the caval involvement is above the right renal vein, which can be isolated. On occasions, the left renal vein will need to be isolated and controlled (Fig. 10.5). It is important to mobilize (and if necessary, ligate) the small hepatic veins draining directly into the vena cava below the main hepatic outflow tract. Isolation of the suprahepatic cava can be done either below or above the diaphragm. Often only temporary proximal occlusion is required of the suprahepatic cava. For more extensive invasion, more formal isolation is necessary. If tumor thrombus extends above the hepatic veins into the atrium, then hypothermic cardiac arrest with cranial perfusion is now the preferred approach. The importance of mobilization of the cava posteriorly cannot be overemphasized. Judicious use of a vein retractor on the right side is helpful, with clear identification of any lumbar veins draining into the posterior vena cava. On the left side, if tumor extends into the renal vein, it often stops at the right side of the aorta if the vein passes posteriorly. When the cava must be resected, the utilization of a vascular stapler superiorly has improved the safety of the procedure. If caval involvement is limited, a limited resection with a patch to the vena cava ensures caval continuity [6].

In a patient with a suprarenal infrahepatic tumor thrombus, tumor usually can be extracted with isolation of the cava and without caval resection. This procedure requires extensive mobilization with temporary occlusion of the inferior vena cava below the hepatic veins and above the renal veins (Fig. 10.6a). If the tumor extends to the outflow tract of the right and left hepatic veins, these must be clearly isolated with complete mobilization of the right lobe of the liver to the patient's left (Fig. 10.6b). In this situation and especially when the tumor extends more proximally into the atrium, hypothermic cardiac arrest with cranial perfusion is preferred. Caval resection can be performed above the renal vein with or without resection of the right kidney and isolation of the left renal vein (Fig. 10.6c). If necessary, the left renal vein can be divided with a vascular stapler to allow left renal vein drainage via the left gonadal vein. When thrombus exists in the proximal left renal vein, again division can often be accomplished without loss of the kidney, if the usually distended left adrenal vein enters the renal vein proximal to the gonadal vein (Fig. 10.6d).

Reconstruction of the resected vena cava is a matter of some debate. With minor thrombus, extraction with or without patch repair is the simplest technique [7]. With major, established suprarenal thrombus, simple ligation without reconstruction has been our commonest approach. With diligent attention to perioperative peripheral edema management, long-term results are excellent, with limited lower edema, probably owing to the prior establishment of vena caval collaterals.

Chemotherapy and radiotherapy have not been shown to be of significant benefit, so complete resection is the only potentially curative approach. Every effort should be made to achieve a complete resection at the first operation. Figure 10.7a demonstrates disease-specific survival stratified by completeness of first resection, and Fig. 10.7b shows disease-specific survival stratified by completeness of second resection [5].

Re-resection of recurrent disease should always be considered, given the lack of effective alternatives. Reoperation should be offered if a complete gross resection appears possible. Incomplete resection is rarely of value and should not be planned.

Figure 10.1

Incisions for appropriate access for major adrenal excision. (**a**) A long midline incision or a bilateral or unilateral subcostal incision is preferred for simple or bilateral tumors. (**b**) A long lumbar incision or thoraco-abdominal incision on the right side is preferred for extended resections with mobilization of the liver. (**c**) A left subcostal incision for access to a left adrenal tumor, with ready extension into the left chest for a large or difficult lesion

Figure 10.1

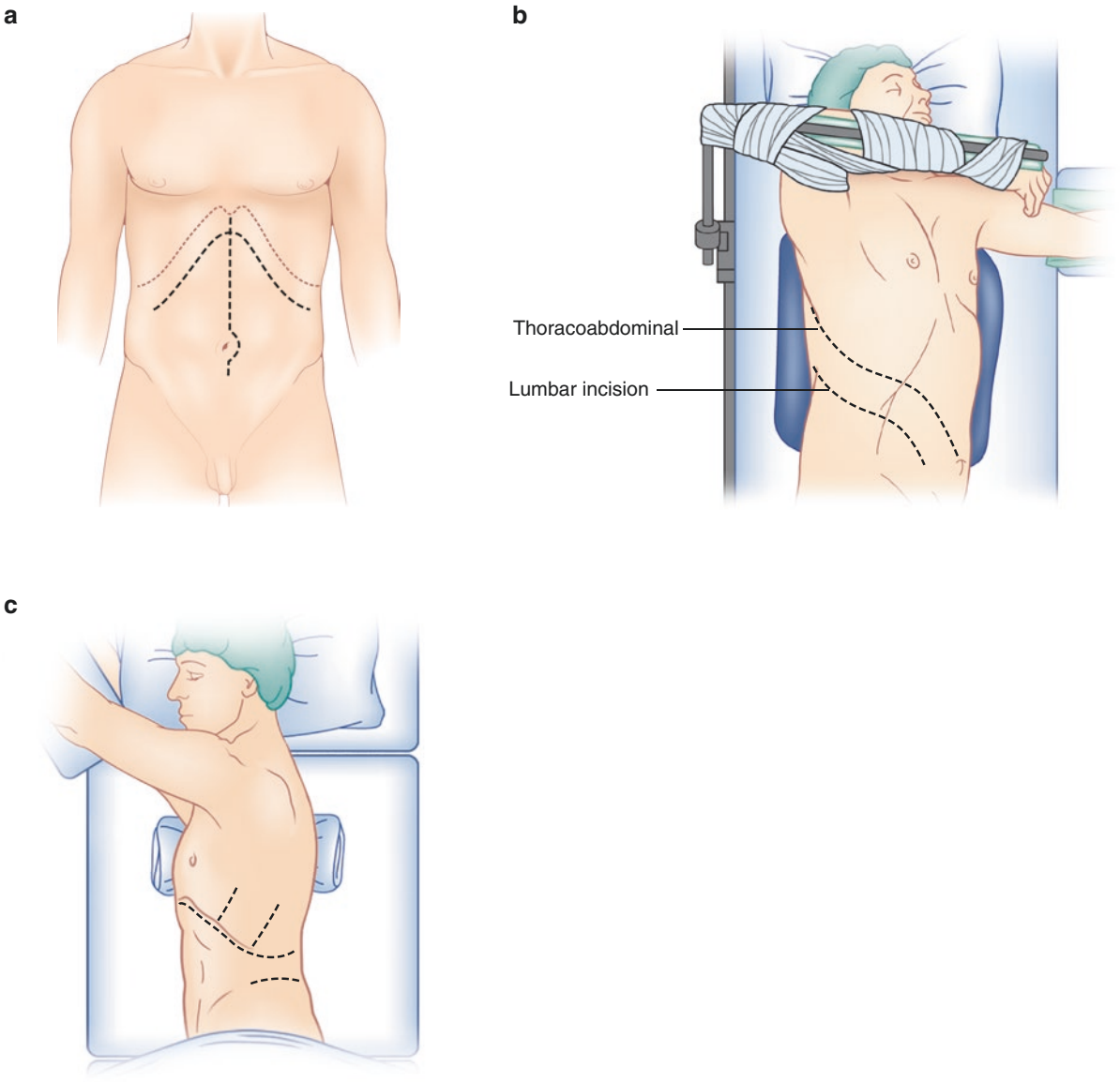


Figure 10.2

For access to the right adrenal, the transverse colon is reflected inferiorly, the duodenum is reflected to the patient's left, and the vena cava is clearly exposed

Figure 10.3

The approach to the left adrenal vein often requires complete mobilization of the spleen and pancreas to gain adequate access

Figure 10.2

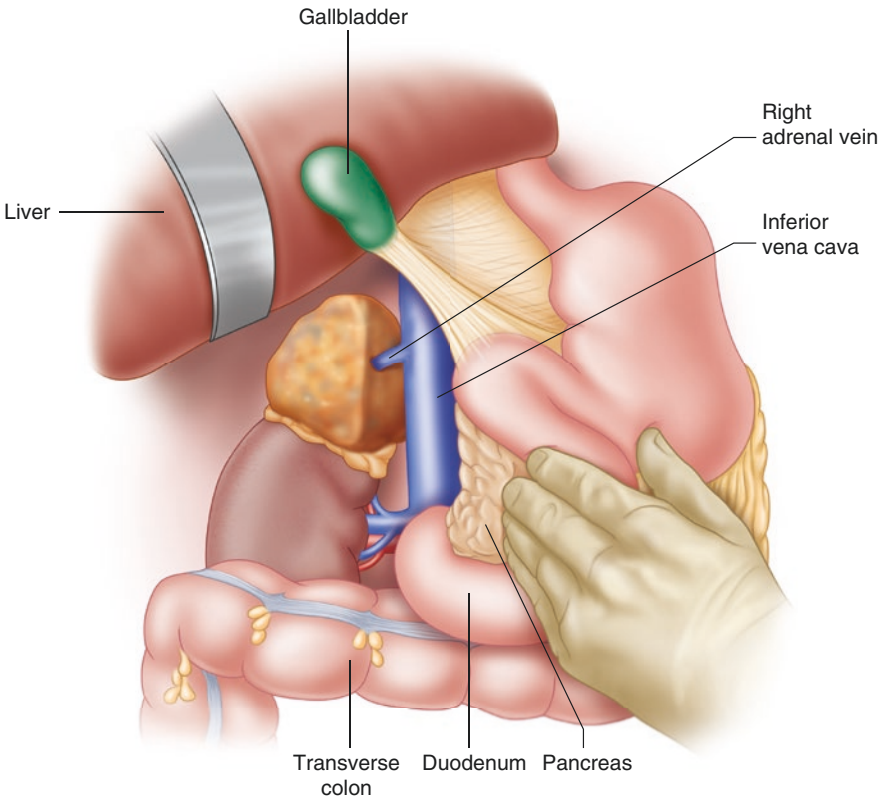


Figure 10.3

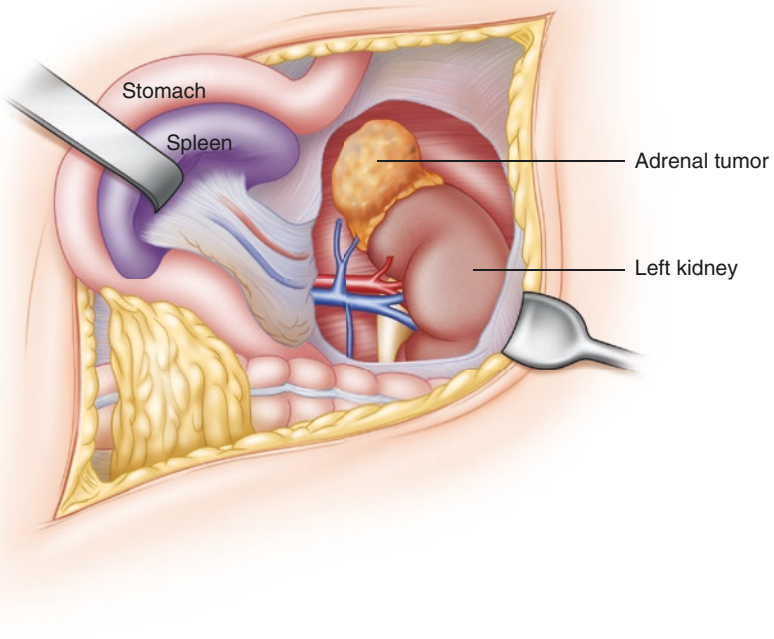


Figure 10.4

The lymphatic drainage of the adrenal, for both the right and left sides

Figure 10.5

Vena cava involvement is usually above the right renal vein, which can be isolated, but occasionally the left renal vein must be isolated and controlled. If the tumor extends close to the hepatic vein outflow, then suprahepatic caval control should be considered. T = tumor

Figure 10.4

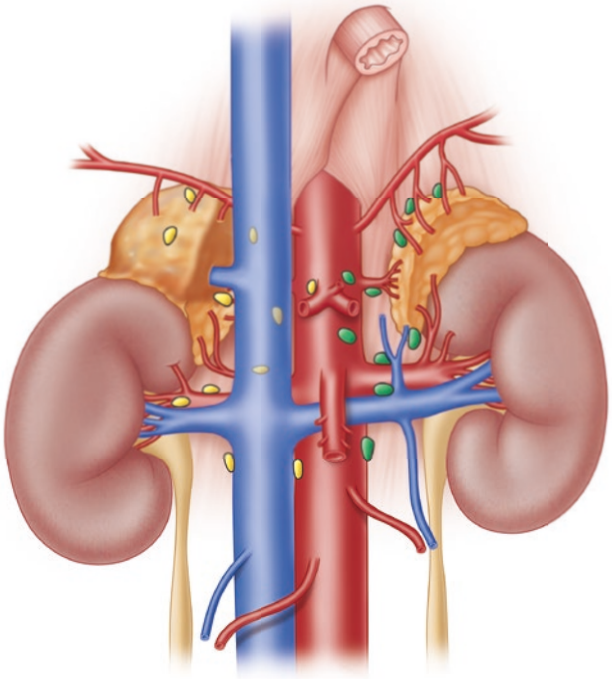


Figure 10.5

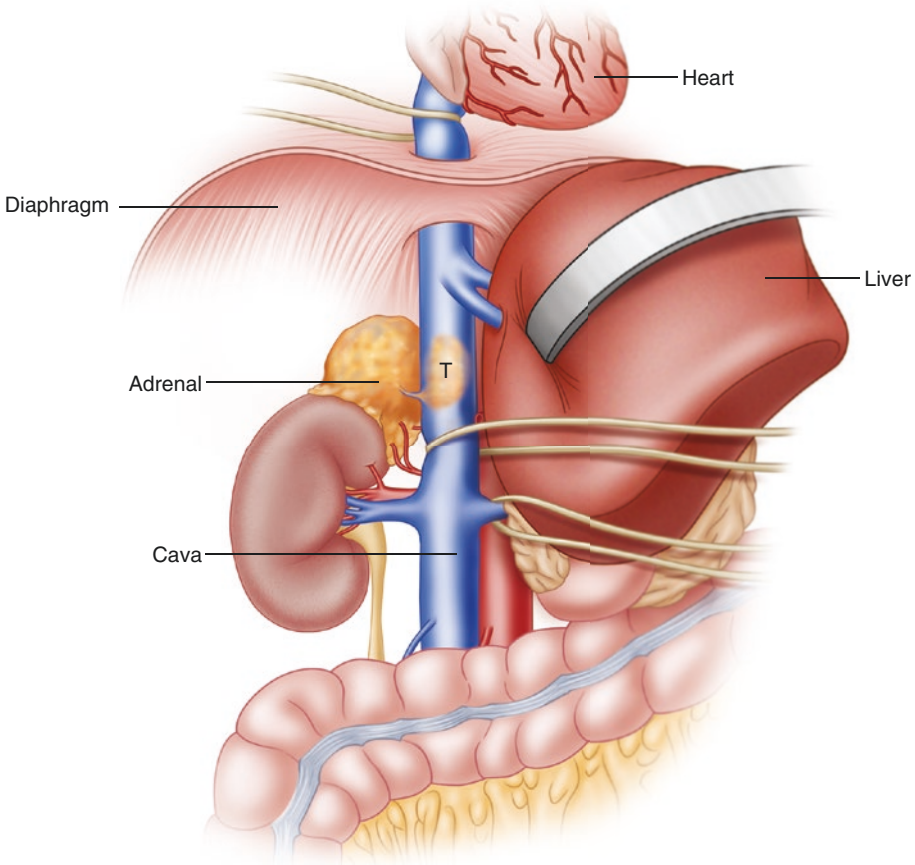


Figure 10.6

Suprarenal infrahepatic tumor thrombus. (**a**) Extraction of the tumor with isolation of the cava and without caval resection requires extensive mobilization with temporary occlusion of the inferior vena cava below the hepatic veins and above the renal veins. (**b**) If the tumor extends to the outflow tract of the right and left hepatic veins, these must be clearly isolated with complete mobilization of the right lobe of the liver to the patient's left. (**c**) En bloc caval and tumor resection with or without the right kidney is necessary (i.e., adrenal vein intact). Caval resection can be performed above the renal vein with or without resection of the right kidney and isolation of the left renal vein. If tumor extends below the right renal vein, then the right kidney must be removed en bloc. (**d**) If thrombus exists in the proximal left renal vein, division often can be accomplished without loss of the kidney if the usually distended left adrenal vein enters the renal vein proximal to the gonadal vein

Figure 10.6

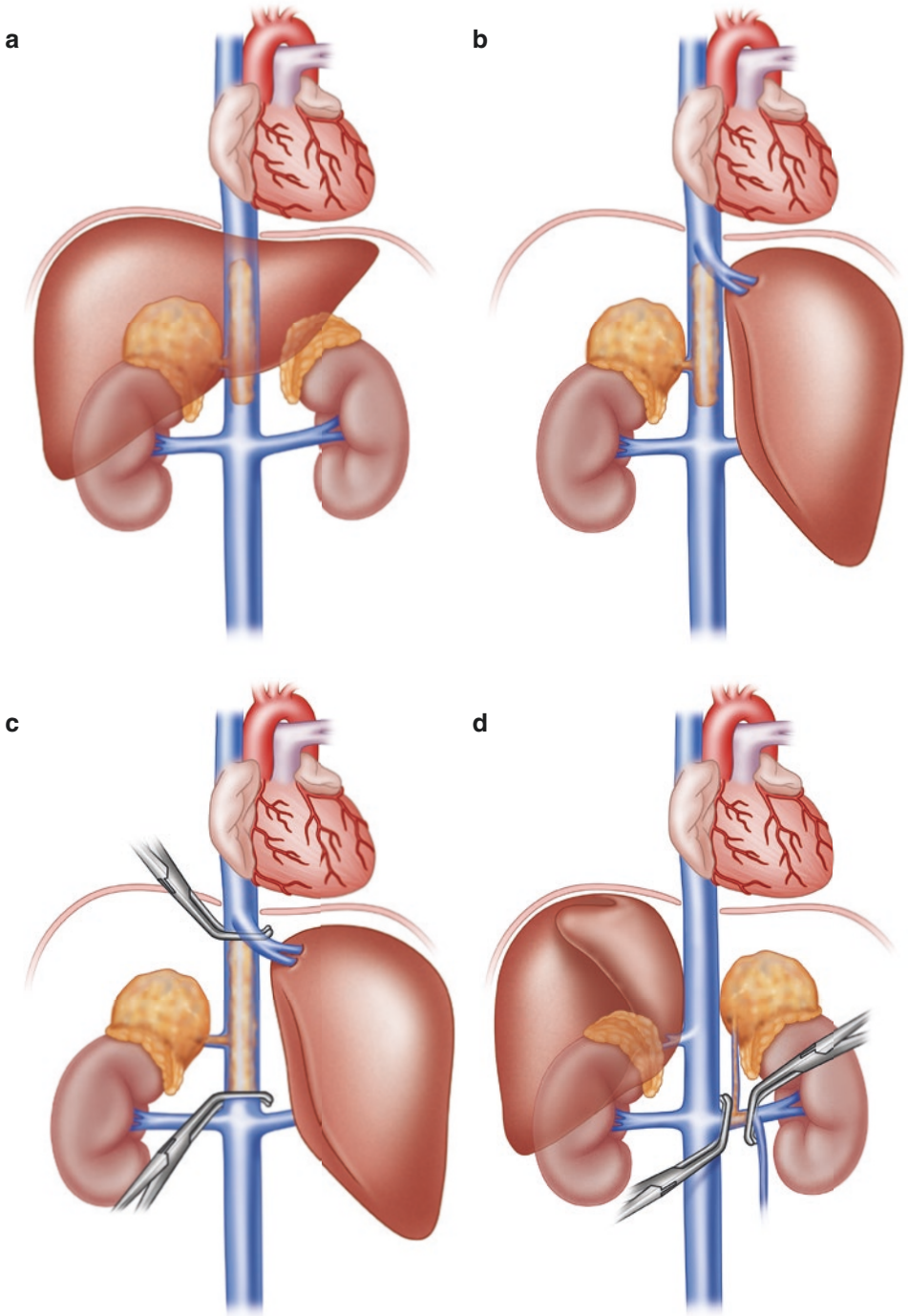
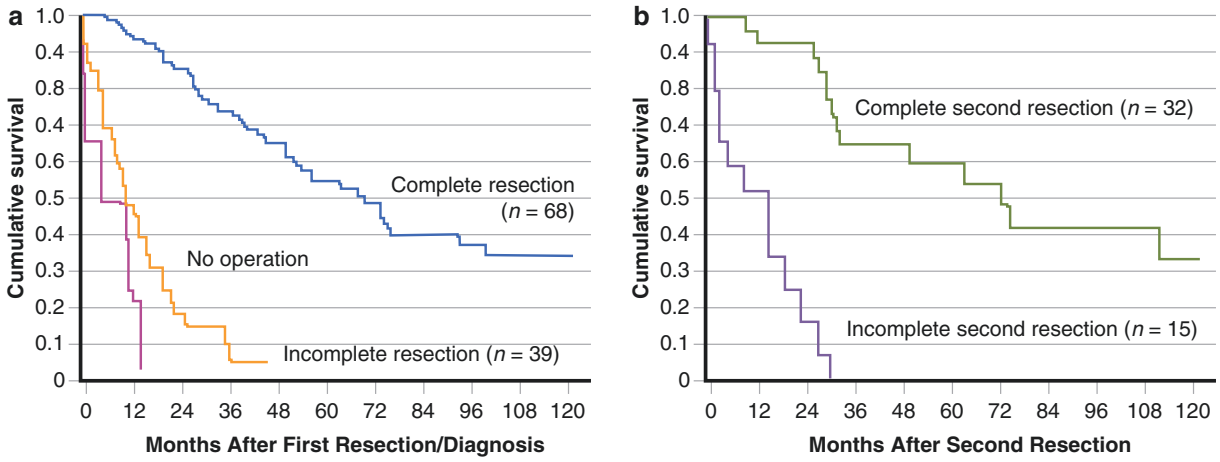


Figure 10.7

Disease-specific survival in patients undergoing resection for adrenocortical carcinoma. (**a**) Survival stratified by completeness of first resection. (**b**) Survival stratified by completeness of second resection (From Schulick and Brennan [5]; with permission)

Figure 10.7


a
Cumulative survival
1.0
0.4
0.8
0.4
0.6
0.5
0.4
0.3
0.2
0.1
0
Complete resection
(n = 68)
No operation
Incomplete resection (n = 39)
0 12 24 36 48 60 72 84 96 108 120
Months After First Resection/Diagnosis
b
Cumulative survival
1.0
0.4
0.8
0.4
0.6
0.5
0.4
0.3
0.2
0.1
0
Complete second resection (n = 32)
Incomplete second resection (n = 15)
0 12 24 36 48 60 72 84 96 108 120
Months After Second Resection

10.3 Results and Conclusions

Open adrenalectomy is currently mandatory for large, malignant adrenal tumors. The approach is similar to other cancer operations. Complete local resection with skeletonization of major vessels and encompassing nodal dissection should be performed whenever possible. Complete resection of the primary tumor is essential to offer any possibility of long-term survival. Surgeons should be aware of the common problem of intravenous vascular extension by tumor thrombus. With conventional imaging, recognition of this extension, with isolation and resection of major vessels, is feasible and safe. The most challenging cases are those that have been explored but did not undergo resection, usually on account of intraoperative hemorrhage. As with most tumor surgery, the first operation is the easiest and the most likely to have a favorable impact on long-term survival. Once tissue planes have been dissected, they are lost, and adherence to surrounding structures becomes inevitable. Poorly placed or aggressive biopsy at the time of an initial, abandoned resection often leads to multifocal or disseminated persistence or recurrence. At any reoperation, resection of adjacent viscera can be the expected norm.

Overall 5-year survival for patients with resected adrenocortical cancer is 30–40%. Patients presenting with early-stage disease (I & II) have a 5- year survival of 60%, but those with stage III/IV have a dismal 5-year survival below 10%. Complete resection of the primary tumor is essential to offer any possibility of long-term survival. It is important to emphasize that re-resection of local and systemic recurrence can be associated with 5-year survival of 50% and should be considered in most patients with recurrence.

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Posterior Adrenalectomy

11

Douglas L. Fraker

11.1 Introduction

Surgery of the adrenal gland has a fairly short history, as the understanding of the functional diseases of the adrenal required sophisticated biochemical techniques, and identification of small- to moderate-sized tumors was aided by the development of cross-sectional imaging techniques [1]. The adrenal glands are almost equidistant from the anterior surface, the lateral surface, and the posterior surface of the skin. In the era before laparoscopic surgery, therefore, adrenalectomy could be performed through a transabdominal approach, a flank approach, or a posterior approach [2] (Fig. 11.1).

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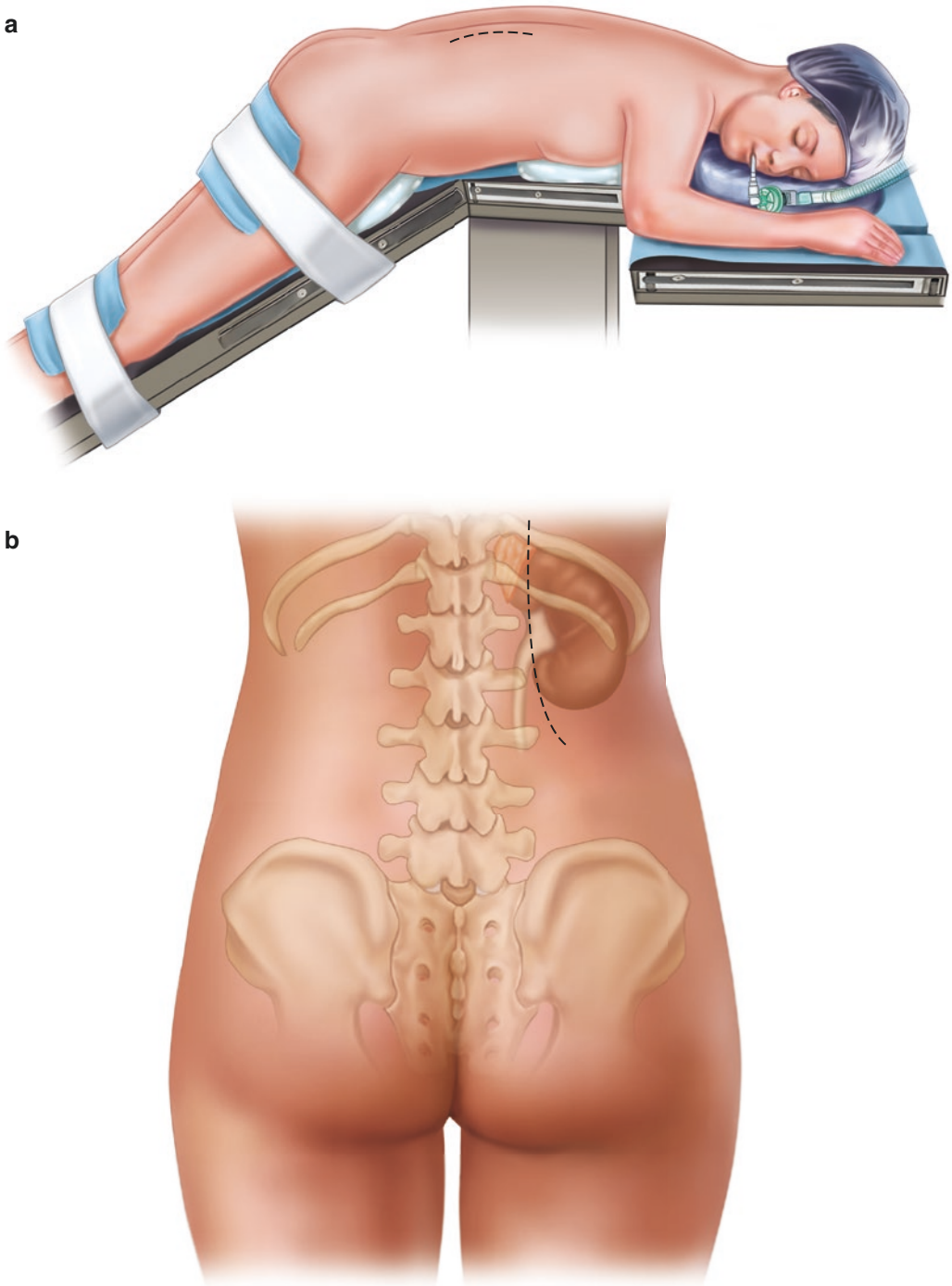
J.R. Howe (ed.), *Endocrine and Neuroendocrine Surgery*, Springer Surgery Atlas Series, DOI 10.1007/978-3-662-54067-1_11

Figure 11.1

(a) Prone positioning for posterior adrenalectomy with the table flexed; the dotted line designates the skin incision. (b) The skin incision is made vertically from the 10th rib and curved slightly towards the iliac crest

Figure 11.1



11.2 Needs and Indications

Indications for adrenal resection have been consistent across all eras of adrenal surgery. Neoplasms of the adrenal cortex are categorized as either functional or nonfunctional. Aldosterone-producing tumors leading to Conn's syndrome (resulting in hypertension with significant hypokalemia) involve unilateral adrenal adenoma in 70–75% of patients. Surgery is indicated on the basis of imaging plus adrenal vein sampling to identify precisely the unilateral source of the excess aldosterone. Aldosteronomas are uniformly benign and small, almost never exceeding the size of 3 cm. Unilateral primary adrenal Cushing's syndrome is due to either adrenocortical adenomas or adrenocortical carcinomas. Larger lesions with associated Cushing's syndrome have a higher tendency for malignancy. Patients are identified by signs and symptoms of excess cortisol, with high 24 h urinary free cortisol and suppressed ACTH. Primary pigmented nodular adrenal disease and adrenal macronodular hyperplasia are rare familial causes of bilateral primary adrenal Cushing's syndrome and can be approached by bilateral adrenalectomy. Patients with pituitary Cushing's disease who have failed one or more transsphenoidal resections of their pituitary gland, with or without salvage attempts by gamma knife radiation, may be eligible for bilateral adrenalectomy to control severe symptoms.

Nonfunctional adrenocortical neoplasms (or so-called adrenal incidentalomas) have become commonly identified by the widespread use of cross-sectional imaging studies. Their incidence increases with age; in general, between 3% and 5% of patients receiving CT or MRI scans have some adrenal nodular disease, as do up to 7% of elderly patients. Most of these lesions are small, and once it is proven by biochemical testing that they do not make catecholamines or steroid hormones, their management depends on the size of the lesion and its rate of growth in serial imaging studies. In the current laparoscopic era, an indication for surgery for a nonfunctional adrenal cortical neoplasm would be a cutoff size $\geq$4 cm, or significant growth over a short period on sequential scans. Because there is no true curative treatment for adrenocortical carcinoma other than surgical resection, vigilant follow-up and appropriate resection is essential in managing these lesions.

Tumors of the adrenal medulla (pheochromocytomas) uniformly produce some level of catecholamine products, which can be measured by plasma catecholamines and metanephrines, or by urinary catecholamines, metanephrines, and vanillylmandelic acid (VMA). These patients are at risk for hypertensive crises and consequences such as myocardial infarctions, acute hypertensive cardiomyopathy, or cerebral vascular events. Any suitable surgical candidate with a biochemically identified pheochromocytoma should undergo adrenalectomy for resection of this potentially lethal lesion after appropriate preoperative alpha blockade.

Prior to the introduction of either laparoscopic transabdominal adrenalectomy or retroperitoneoscopic posterior adrenalectomy, the open posterior approach to the adrenal gland was preferred for small, functional lesions [2]. These lesions included aldosteronomas, small adrenocortical neoplasms causing Cushing's syndrome, and even small lesions with metastatic disease. This approach is ideally suited for bilateral adrenalectomy of normal or modestly hypertrophied glands in the setting of failed treatment of pituitary Cushing's, because these patients have a great degree of truncal obesity and positioning allows a fairly straightforward bilateral approach. Limitations of posterior adrenalectomy relate to larger tumor size. The posterior approach leaves a fairly narrow window of view, so tumors generally larger than 5–6 cm are not easily accessed by this exposure. Because virtually all lesions smaller than 5–6 cm can be successfully removed by either transabdominal laparoscopic adrenalectomy or retroperitoneoscopic posterior video-assisted adrenalectomy, the posterior approach to the adrenal should be viewed somewhat as a historical operation. There are rare indications for utilizing this approach today, however, despite the availability of other, minimally invasive techniques. For example, the use of video-assisted techniques may be quite challenging in patients who are very morbidly obese due to pituitary Cushing's, because of their body habitus.

11.3 Surgical Technique

In 1936, Young [3] initially described the posterior approach for the resection of the adrenal glands. Patients are positioned completely prone on the operating room table with their arms stretched over their heads (Fig. 11.1a). Rolls are placed under the pelvis and under the chest/axillary area with a gap between the padding to allow the intra-abdominal contents to hang forward and pull away from the retroperitoneum. All pressure points are padded, with care taken to provide padding for the face area with the endotracheal tube.

Incisions are made in a hockey-stick manner, as described by Young (Fig. 11.1b). In the prone position, one can palpate the spinous processes of the lumbar vertebrae even in obese patients and count the ribs. The 10th, 11th, and 12th ribs

should be identified by deep palpation and marked with a pen. Attempts should be made to palpate the paraspinus muscles, specifically the sacrospinalis muscle, as the optimal position of the vertical portion of the incision is just on the lateral border of that muscle, but it may not be identifiable in obese patients with a considerable adipose layer. One should make a vertical incision from the 10th intercostal space along the lateral border of the sacrospinalis muscle, approximately four fingerbreadths lateral to the spinous processes. When extending the incision inferiorly below the 12th rib, the incision should be gently angled laterally towards the posterior superior iliac spine.

The incision is carried sharply down to the fascial part of the latissimus dorsi muscle, which lies under this hockey-stick incision (Fig. 11.2). At the superior aspect, one may have to divide some muscle fibers and then, with the subcutaneous tissue parted again, feel the sacrospinalis muscle. Incise to the deep lumbar fascia just on the lateral border of the sacrospinalis muscle. The sacrospinalis muscle is retracted medially and the origins of the 12th and 11th ribs are palpated (Fig. 11.3a). Once the 12th rib is identified, the soft tissue is opened down to the periosteum (Fig. 11.3b), which is then stripped with an elevator. This rib is resected all the way to the edge of the spine. Attempts can be made to preserve the neurovascular bundle at the inferior margin of the 12th rib, or at least the nerve, as division will lead to numbness and laxity of the flank muscles. In patients of short stature and often in Cushing's patients with considerable truncal obesity, the 11th rib may need to be excised in a similar manner. If two ribs are excised, then the neurovascular bundle and 12th rib must be divided, which will result in numbness along the dermatomal distribution of that nerve root. With this exposure, the anterior lumbar dorsal fascia is incised and the retroperitoneal space is identified and visualized, with variable degrees of spongy adipose tissue (Fig. 11.4). This initial incision into the lumbar dorsal fascia is made towards the inferior portion of the incision, to try to avoid entering the chest cavity. With gentle blunt dissection, one should next identify the diaphragm and gently reflect the pleura cephalad (Fig. 11.5).

Next, the diaphragm muscle is partially divided towards the spine using cautery (Fig. 11.6), then Gerota's fascia is opened (Fig. 11.7). Blunt dissection of the fat is carried out gently along the diaphragm, while pulling the kidney down. On the right side, the liver will be encountered (Fig. 11.8a) and the adrenal gland identified below this and above the kidney. It will have a more orange hue than the lighter yellow fat and more compact structure. The posterior approach is somewhat ideal, as the adrenal tends to lie close to the posterior lumbar sacral fascia and there is less fatty tissue to dissect than when coming from the anterior approach. By gently retracting the kidney inferiorly, the adrenal is pulled away from the diaphragm. Because of this ability to improve adrenal exposure by renal retraction, it is important to divide the superior, and lateral attachments of the adrenal gland initially, so as not to disconnect the kidney from the adrenal. This dissection should be done with a harmonic scalpel, dividing the inferior phrenic artery (Fig. 11.8b). Previously, this was done with hemoclips, as placing ties along these small vessels is challenging on account of their depth and limited exposure. The medial dissection should be approached with caution. The IVC is identified and then the horizontally oriented adrenal vein dissected out. Exposure of the right adrenal vein is more challenging than on the left side, as it is shorter and more superiorly located toward the diaphragm. It generally arises from the upper one third of the medial adrenal gland but again is more posterior and should be dissected, tied, or clipped. Control and division of the adrenal vein is the most crucial part of the operation, as venous injury with significant bleeding is very difficult to expose and repair via the posterior approach. The vein should be doubly clipped on the IVC side and divided (Fig. 11.8c). Additional attachments can then be taken down with the energy device, and the adrenal separated off the kidney and removed.

On the left side, identification of the adrenal vein with this exposure is relatively straightforward. It comes off the posteromedial aspect of the adrenal gland and is quite visible from the posterior approach, coming off the inferior phrenic vein (Fig. 11.9a). This vein can be dissected free and either tied with silk ties or controlled with multiple hemoclips. The remaining arterial branches from the inferior phrenic, aorta, and renal artery can be divided by circumferential dissection with the energy device (Fig. 11.9b). Care should be taken to not injure the renal artery of the vein during this dissection, and then the adrenal gland can be delivered.

In a few patients, the thoracic cavity may be entered, exposing the pleura and lung. This posteriolateral area is a very thin part of the diaphragm, and simple closure with a running absorbable suture is possible. The lung is virtually never injured; evacuation of air can be accomplished with a Valsalva maneuver and a drainage tube. The lumbodorsal fascia is closed with interrupted absorbable suture (Fig. 11.10). The subcutaneous tissue may be approximated and the skin is closed.

Figure 11.2

Division of the skin and subcutaneous tissues reveals the posterior lumbar dorsal fascia

Figure 11.3

The 12th rib is dissected out and then the periostium is opened and reflected off of the rib (*inset*)

Figure 11.2

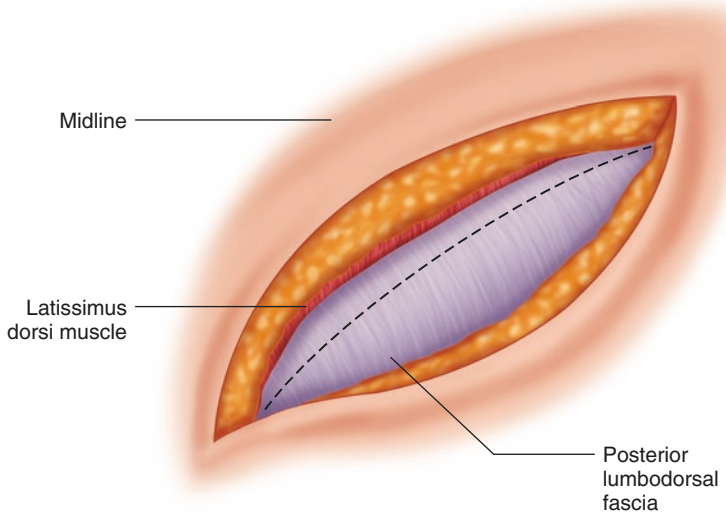


Figure 11.3

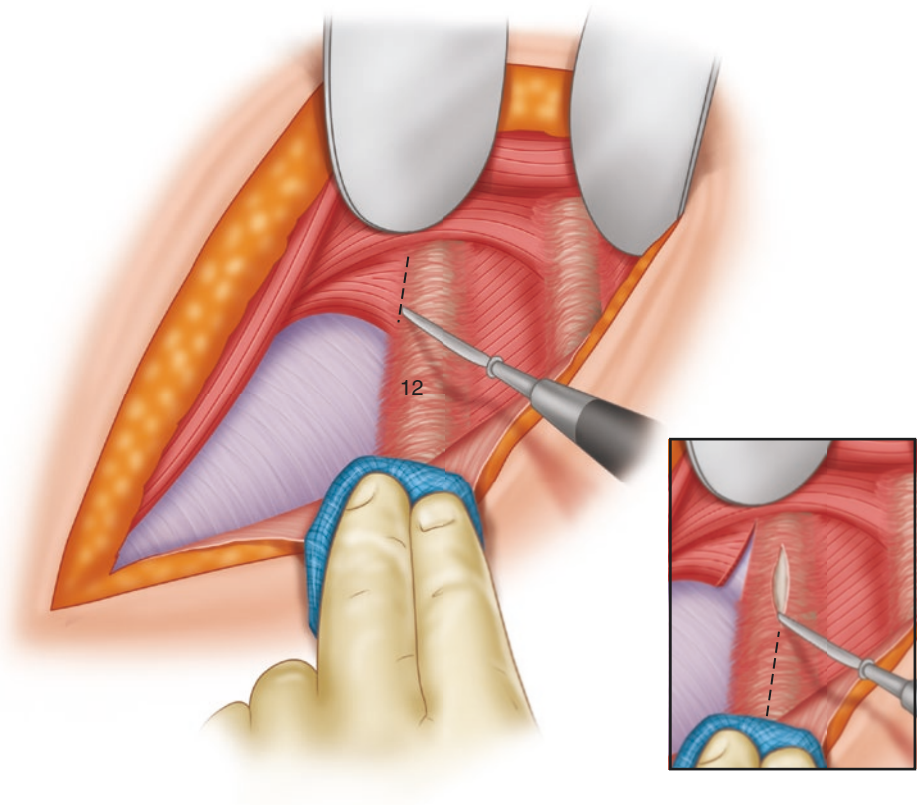


Figure 11.4

The rib is resected as close to the spinous process as possible after dissecting out the neurovascular bundle. Efforts should be made to preserve the nerve while the vein and artery may be ligated and divided. The anterior lumbar dorsal fascia is incised

Figure 11.5

The pleura is dissected cephalad off the diaphragm

Figure 11.4

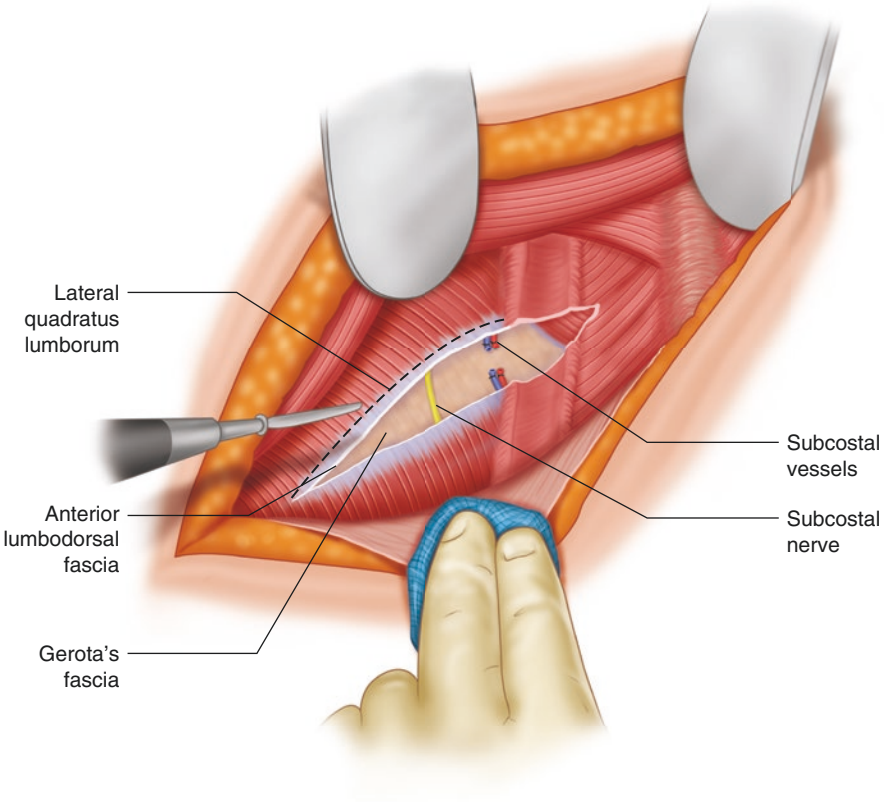


Figure 11.5

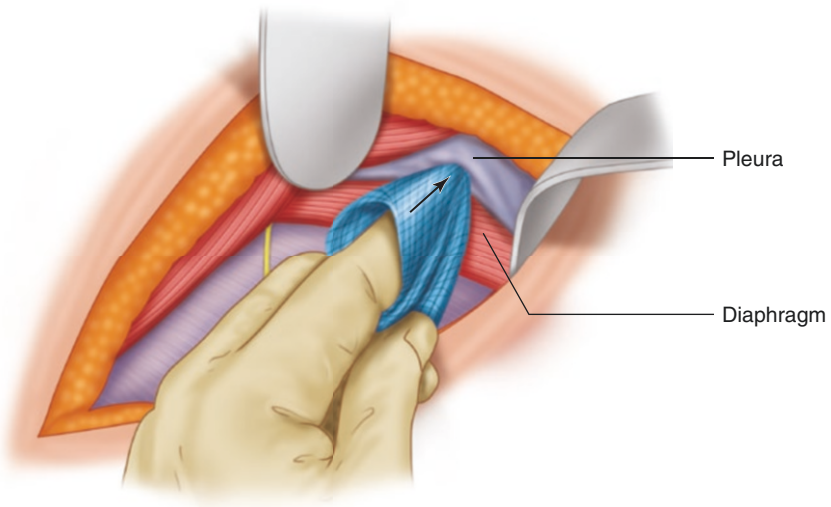


Figure 11.6

The diaphragm is partially divided with cautery medially

Figure 11.7

Gerota's fascia is incised, exposing the perinephric fat

Figure 11.6

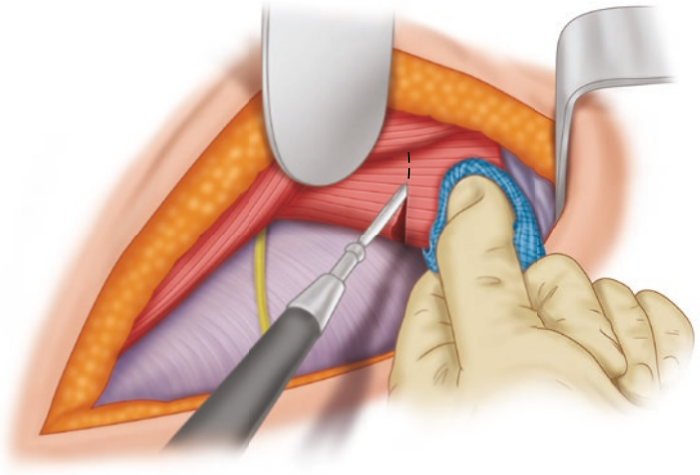


Figure 11.7

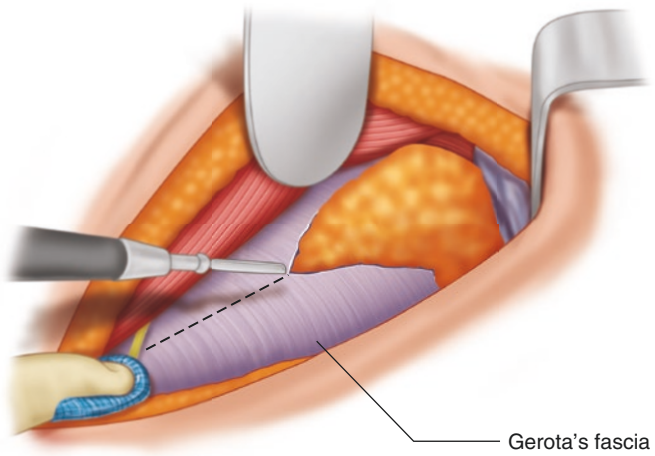


Figure 11.8

On the right side, the fat is bluntly dissected off the diaphragm pulling it down with the kidney (**a**). Superiorly, inferior phrenic vessels are taken with an energy device (**b**). The medial aspect is approached carefully, identifying the IVC, then the large adrenal vein coming off horizontally. This is doubly clipped and divided (**c**)

Figure 11.8

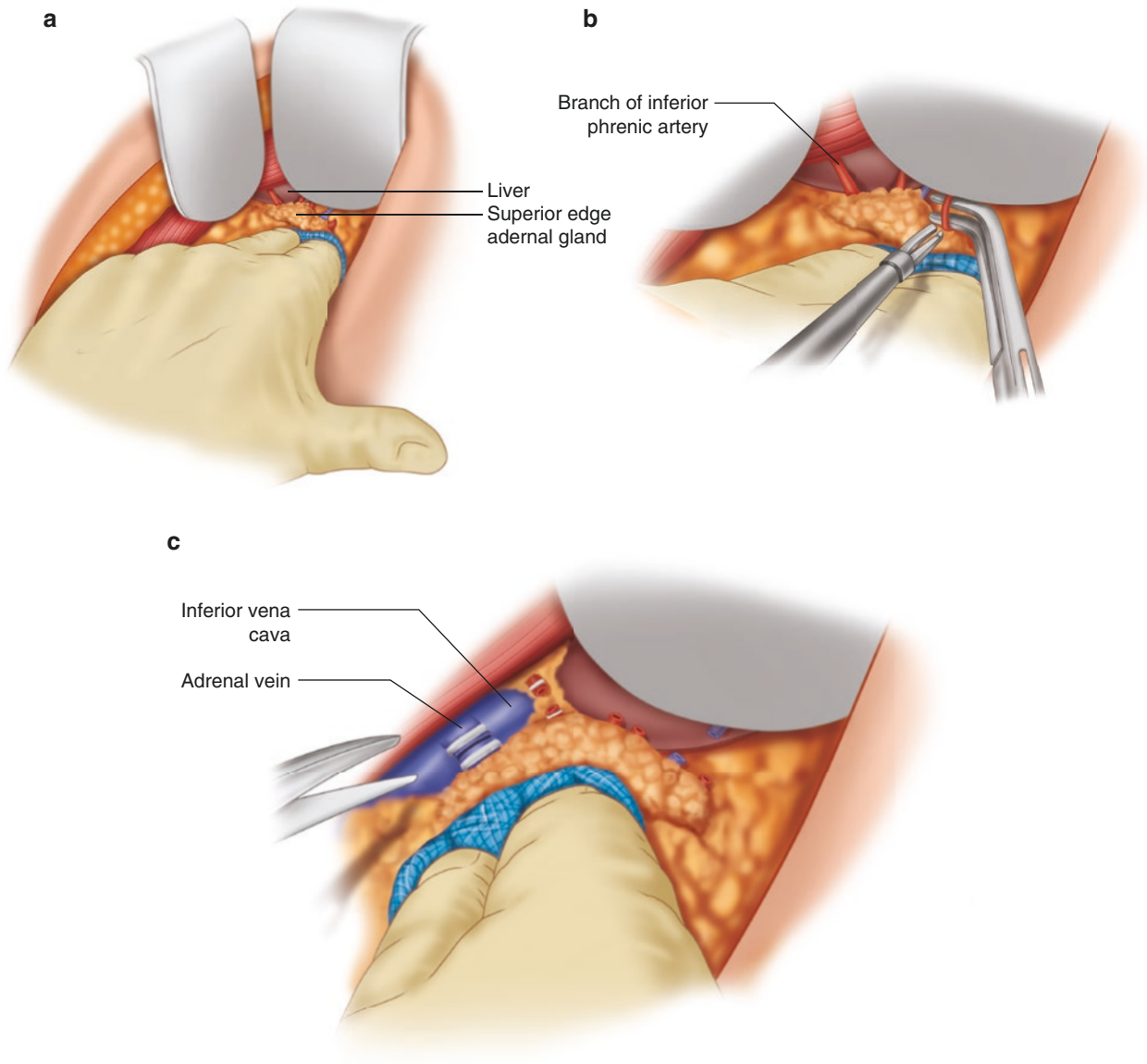

a
Liver
Superior edge
adernal gland
b
Branch of inferior
phrenic artery
c
Inferior vena
cava
Adrenal vein

Figure 11.9

On the left side, the inferior phrenic vein is identified (**a**), then dissected out to identify the left adrenal branch coming off superolaterally (**b**)

Figure 11.9

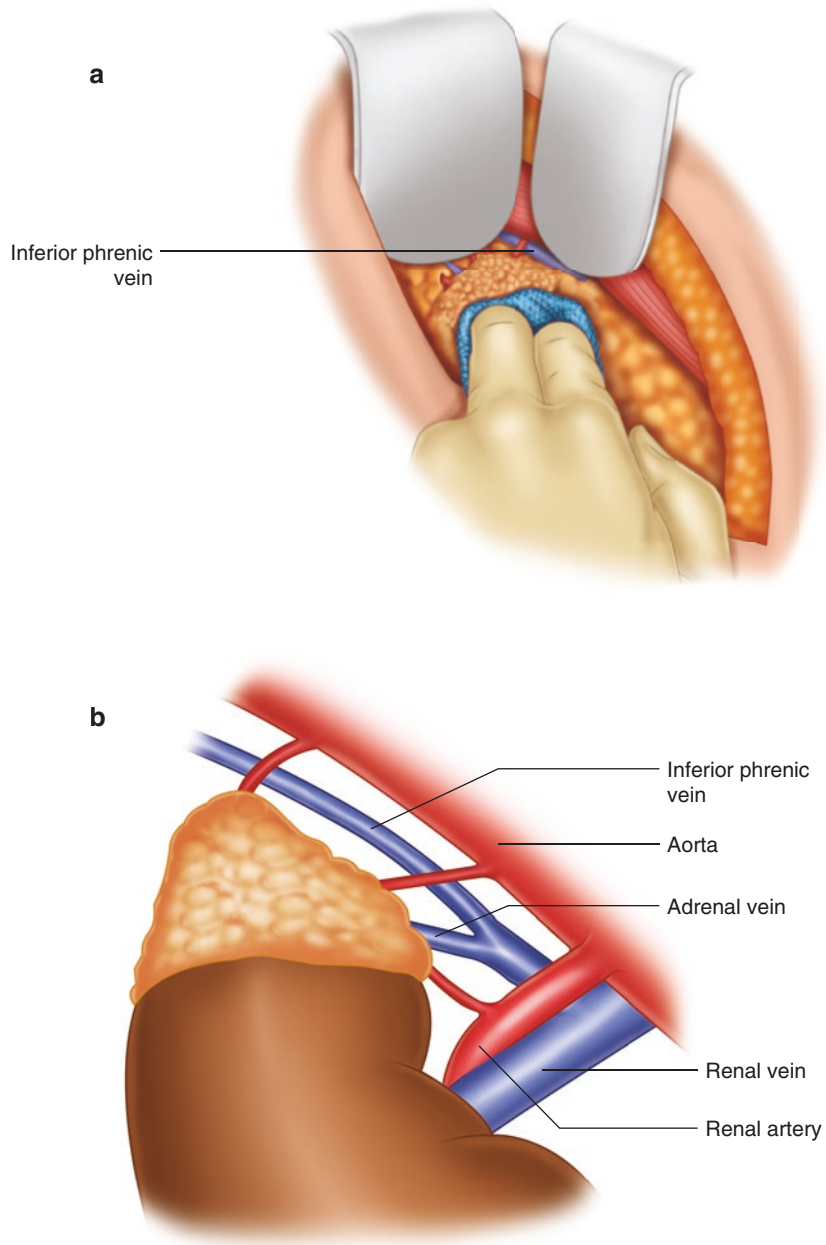
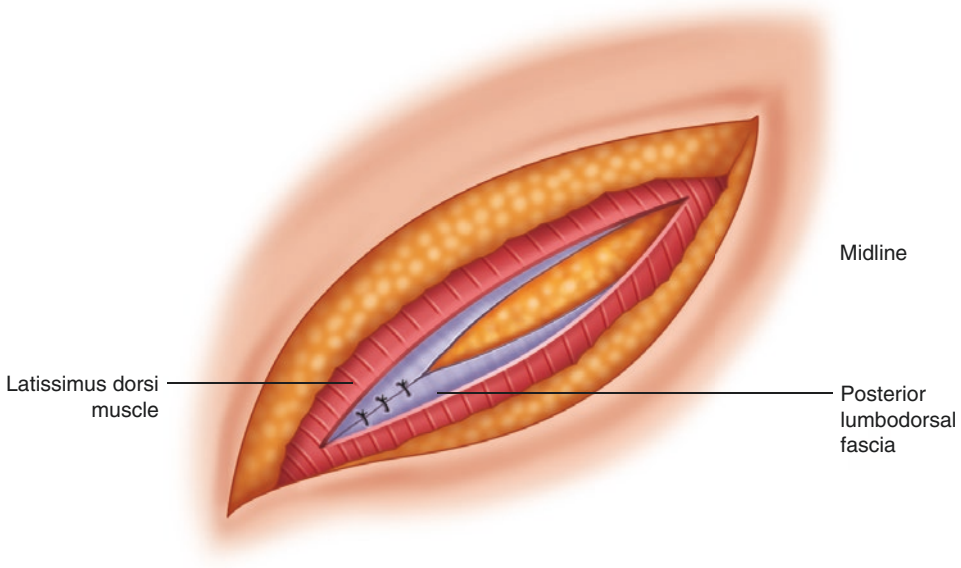

a
Inferior phrenic vein
b
Inferior phrenic vein
Aorta
Adrenal vein
Renal vein
Renal artery

Figure 11.10

Closure of the posterior lumbodorsal fascia with absorbable sutures

Figure 11.10


Midline
Latissimus dorsi muscle
Posterior lumbodorsal fascia

11.4 Results and Conclusions

Open adrenalectomy using a posterior approach versus an anterior approach was compared in several high-volume institutional series throughout the 1970s and 1980s. These series concluded that the posterior approach was preferred because it was safer, had less postoperative discomfort, and led to shorter hospital stays. A comparative approach of a large series of patients from the Mayo Clinic demonstrated a hospital stay of 9 days for a unilateral resection with an anterior approach and 5 days with a posterior approach [2]. Blood transfusions were necessary in 22% of patients with the anterior approach and only 1% of patients with the posterior approach. One should keep in mind this was not a randomized series, and the patients selected for the anterior approach uniformly had larger tumors. The operating time was virtually identical in this series of patients, 95 min for an anterior approach and 85 min for the posterior approach [2]. Entry into the diaphragm and chest cavity occurred in 25% of patients, which was not really a significant complication in terms of morbidity for patients.

A large series of 105 posterior adrenalectomies from the University of Lille, France, showed that this is a very safe operation [4]. There were no intraoperative deaths. There was one minimal inferior vena cava tear, and 13 patients had their chest cavities entered. Of 105 patients, six received a blood transfusion, and the mean operative time was 132 min. The average hospital stay in this series (mostly from the 1970s to 1990s) was 7 days. The majority of these patients had aldosteronomas or small primary adrenal Cushing's neoplasms.

The posterior approach versus anterior approach was analyzed retrospectively at the National Institutes of Health (NIH) in a large series of patients undergoing bilateral adrenalectomy for failed pituitary Cushing's disease [5]. The operative time was comparable at approximately 200 min. Blood loss and transfusions were identical. Patients recovered much more quickly after undergoing the posterior bilateral adrenalectomy approach: the mean time to a full diet decreased by 50%, and hospital time was shorter for the posterior approach. This specific patient population reported a very high incidence of sometimes debilitating back pain from bilateral open posterior adrenalectomy, however. Because these patients were all suffering from severe Cushing's syndrome, they may have had poor wound healing and a body habitus that made them more susceptible to this acute complication. Of the patients with a posterior approach, 81% suffered from chronic incision-related pain, compared with 7% with the anterior approach [5].

Since the introduction of minimally invasive techniques circa 1990, the focus has become the comparison of open versus laparoscopic procedures, as opposed to open posterior versus open anterior. Several institutional studies have reported similar results. Specifically, the minimally invasive laparoscopic approach had much shorter hospital stays, much greater patient satisfaction, and a faster return to normal activity. The Mayo Clinic reported a case-control study with a longer operating time to do a laparoscopic approach and higher operating room charges [6]. A similar study from England reported that the operative time was almost double for the laparoscopic approach compared with an open posterior approach [7]. However, the mean hospital stay was reduced from 8 to 3 days after laparoscopic adrenalectomy.

Again, the open posterior adrenalectomy procedure should be viewed as a historical operation. The longer operating time reported in the early comparisons of open posterior adrenalectomy to laparoscopic adrenalectomy clearly represent surgeons and institutions in the early part of the learning curve for the laparoscopic approach. Both the operative times and the hospital length of stay with current series and techniques are significantly less than in these early reports. There are now few indications for the open posterior adrenalectomy. If a large adrenal tumor is not amenable to laparoscopic or retroperitoneoscopic resection, it should be approached with an anterior open resection. This author has not performed the open posterior adrenalectomy in more than 20 years, despite having a very high-volume adrenalectomy practice.

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Laparoscopic Transabdominal Lateral Adrenalectomy

12

Michael J. Campbell and Quan-Yang Duh

12.1 Introduction

Adrenal tumors can be benign or malignant and can range in size from small adenomas to large carcinomas. Although some adrenal tumors are found as part of a clinical workup for hormone hypersecretion or local symptoms, an increasing number of adrenal tumors are found on abdominal imaging done for unrelated symptoms and are termed "incidentalomas."

In general, there are two indications for adrenalectomy for an adrenal tumor: hormone production or concern for malignancy. Hormone production occurs mostly as Cushing's syndrome (hypercortisolism), pheochromocytoma, or hyperaldosteronism. The most common malignancy of the adrenal glands is metastasis. Adrenal cortical cancer is rare, but it should be considered with large tumors or tumors that have suspicious radiographic features such as irregular borders, local invasion, or a noncontrast CT attenuation greater than 10 Hounsfield units [1].

Since Gagner et al. first reported a successful laparoscopic adrenalectomy in 1992 [2], laparoscopic resection of adrenal tumors has grown exponentially and is now considered routine for most cases [3]. Laparoscopic adrenalectomy has many advantages over the open approach, including shorter hospitalization, less pain, less operative blood loss, and fewer complications [1]. Laparoscopic adrenalectomy may be contraindicated in patients with a non-correctable coagulopathy, intracranial hypertension, or cardiac and respiratory disorders. There is no absolute size criterion for determining which tumors can be resected laparoscopically. Successful laparoscopic resection of large tumors depends on technical considerations (such as the side of the tumor, patient size, and prior abdominal operations) and institutional experience. Tumors up to 15 cm can be resected laparoscopically, but the limits of safe laparoscopic resection usually are 8–10 cm on the left side and 6–8 cm on the right [4]. The role of laparoscopic adrenalectomy in the management of adrenocortical cancers is controversial [5].

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12.2 Surgical Technique

Laparoscopic adrenalectomy is undertaken using general anesthesia with tracheal intubation and muscle relaxation. A Foley catheter is placed before turning the patient to the lateral decubitus position. Invasive monitoring such as arterial and central venous catheters may be used, depending on the anticipated hemodynamic fluctuations. An orogastric or nasogastric tube is placed to decompress the stomach. Perioperative antibiotics are generally not necessary, except in patients with Cushing's syndrome. Patients with an aldosteronoma should have their preoperative potassium level checked and hypokalemia corrected. Patients with a pheochromocytoma should be titrated up on alpha blockade for 2 weeks preoperatively and should be volume-repleted with salt loading and increased fluid intake. Patients with Cushing's syndrome may require correction of electrolyte abnormalities and hyperglycemia prior to surgery, with steroid replacement perioperatively. Sequential compression stockings should be used on all patients, and some may need perioperative subcutaneous heparin to minimize the risk of venous thromboembolism.

12.2.1 Laparoscopic Right Adrenalectomy

The patient is placed in a modified left lateral decubitus position (80° angle) with the aid of a bean bag (Fig. 12.1). An axillary roll is placed to protect the brachial plexus. The patient is positioned on the table with the 11th rib over

J.R. Howe (ed.), *Endocrine and Neuroendocrine Surgery*, Springer Surgery Atlas Series, DOI 10.1007/978-3-662-54067-1_12

the "break" in the bed. The bed is then flexed to open the space between the costal margin and iliac crest. A kidney rest can be used to further improve this exposure. Pillows are placed between the patient's legs, which are slightly bent to maintain a neutral position. The patient is secured to the bed with 3-inch cloth tape across the knees, hips, and chest. The patient's left arm is laid outstretched and slightly bent on an arm board and the patient's right arm is flexed at the elbow and positioned on pillows or on an elevated arm board.

Pneumoperitoneum is established using a Veress needle approximately 1-2 cm below the right subcostal margin in the midclavicular line. The intra-abdominal pressure is initially insufflated to 20 mmHg to facilitate safe placement of the initial trocar. Close communication with the anesthesiology team is paramount, specifically regarding a decrease in end-tidal CO_2, possibly indicating a CO_2 embolism. A 10-mm dilating trocar is placed at the initial Veress needle location (T1); the intra-abdominal pressure is decreased to 15 mmHg and a 30°, 10-mm laparoscope is inserted to inspect for liver or bowel injury. Three additional 10-mm trocars are placed 1–2 cm below the subcostal margin (T2–T4), evenly spaced between the midclavicular line and the midaxillary line (Fig. 12.2a). The trocar sites are infiltrated with local anesthetic prior to incising the skin. For large tumors, trocars can be placed further inferiorly or in an "L" pattern to facilitate dissection (Fig. 12.2b).

Both the surgeon and the assistant surgeon stand in front of the patient. The assistant stands more cephalad and controls the fan retractor, which is placed through the T1 port, and the laparoscope, which is inserted through the T2 port. The surgeon uses a laparoscopic hook cautery through the third port (T3) and provides counter-tension using a laparoscopic grasper with a rolled sponge through the most lateral port (T4).

The first step in the operation is to "open the book" by releasing the right lobe of the liver from its peritoneal attachments and the triangular ligament (Fig. 12.3). This is done using hook cautery. A small window is made in the peritoneum overlying Gerota's fascia lateral to the inferior vena cava (IVC) approximately 1 mm off the liver, and the dissection is carried cephalad and caudal in a superficial plane. As the liver is freed, the fan retractor gently pushes the right lobe medially. The IVC is identified ascending superiorly and running behind the caudate lobe of the liver.

Once the surgeon has mobilized the liver off of the adrenal gland, the next step is to identify the medial, superior edge of the triangular adrenal by dissecting the thin attach-

Figure 12.1

Patient positioning for a laparoscopic right adrenalectomy

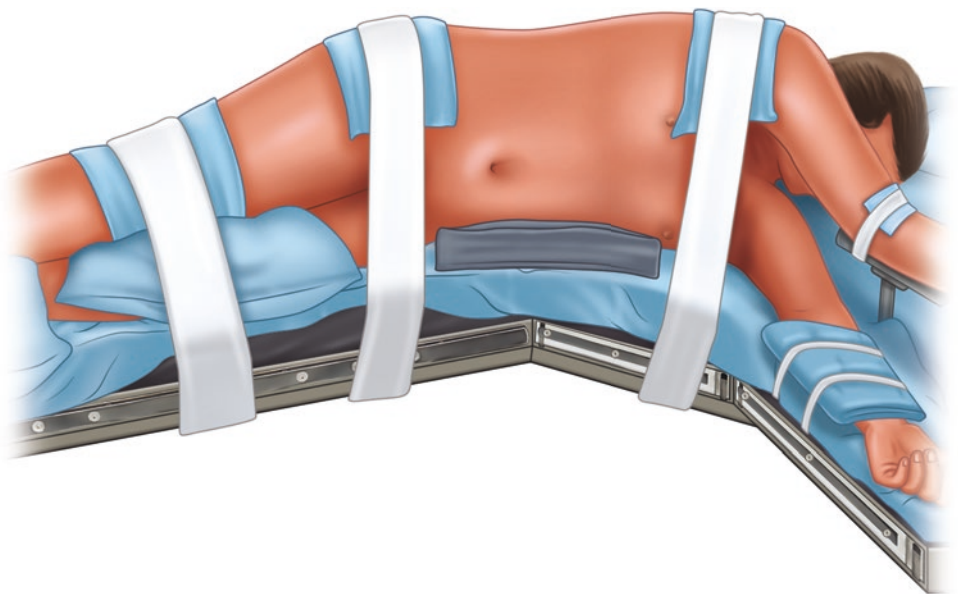
ments between the lateral, posterior edge of the liver and the medial limb of the adrenal gland. The adrenal is evident from its deep golden color. The apex of the adrenal gland's two limbs (medial and lateral) is dissected free (Fig. 12.4), and the surgeon uses hook cautery to continue the dissection inferiorly, working between the medial limb of the adrenal, the liver, and IVC.

The next step is to identify, dissect, and ligate the adrenal vein (Fig. 12.5). The adrenal vein typically drains from the inferior medial edge of the adrenal directly into the IVC. This dissection must be approached with caution because 5–10% of patients will have multiple central adrenal veins and about 5% of patients will have variant drainage into the right hepatic vein or right renal vein [6]. Once the short right adrenal vein is identified, it is dissected circumferentially using a combination of blunt dissection and hook electrocautery. The inclination is to ligate the vein immediately once it has been identified, but we find that continuing to dissect the adrenal gland from the lateral aspect of the IVC allows for more length, therefore facilitating better placement of clips. Once the surgeon has adequate length on the adrenal vein, three clips are placed. The vein is then divided, leaving two clips medially (on the IVC side) and one clip laterally (on the adrenal side). Alternatively, an Endo-GIA™ stapler (Covidien, Mansfield, MA) can be used for large veins. There are often small adrenal arteries deep to the adrenal vein that must be carefully coagulated. The remainder of the retroperitoneal fat between the medial limb of the adrenal and the IVC is then dissected with hook cautery until the surgeon sees the underlying psoas muscle.

Next, the surgeon uses a hook cautery to dissect the inferior edge of the adrenal gland away from the renal vein and hilum (Fig. 12.6). We advocate using hook cautery instead of an ultrasonic scalpel or laparoscopic bipolar device for this portion of the operation because often a superior pole renal artery traverses this plane, and it can be accidentally transected with such devices. The surgeon carries out the dissection from medial to lateral along the inferior edge of the adrenal gland. The right renal vein joins the IVC with a gentle slope just caudal to the line of dissection. Once the adrenal is dissected off the renal hilum and the surgeon sees the dark brown kidney capsule, a laparoscopic bipolar device is used to separate the kidney from the adrenal gland in a clockwise direction.

The final step in the dissection is the separation of the periadrenal fat from the posterior muscle attachments (Fig. 12.7). This is done by gently elevating the specimen anteriorly, using an open-jaw laparoscopic grasper and dividing the attachments using a laparoscopic bipolar device. The

Figure 12.1



dissection is carried from inferior to superior and is performed in a plane that allows the surgeon to separate the periadrenal fat from the underlying psoas muscle and diaphragm. The surgeon must see the underlying muscle to ensure that he is not inadvertently dividing across the adrenal gland, potentially leaving gland and tumor behind.

The specimen is placed into a 4 × 6 inch nylon bag, which is introduced through the lateral (T4) port. The nylon bag with the specimen inside is then brought out through the port, and the port is removed. The skin is protected with towels. The adrenal gland and tumor are then morcellated and removed out of the bag via the 10-mm incision, using ringed

Figure 12.2

(**a**) Trocar sites for laparoscopic right adrenalectomy. (**b**) Placement of trocar sites to facilitate dissection of a large tumor

forceps (Fig. 12.8). Care must be taken to perform this procedure under laparoscopic visualization to avoid damaging the liver, kidney, or bowel during the morcellation process. If the surgeon wishes to remove the specimen intact, then the lateral port site can be enlarged to accommodate it.

After removing the specimen, the lateral-most trocar is reinserted and the adrenal bed is examined for hemostasis. We do not routinely close the fascial defect created using a 10-mm dilating trocar. We do not leave a drain. The skin is closed with absorbable suture and glue.

Figure 12.2

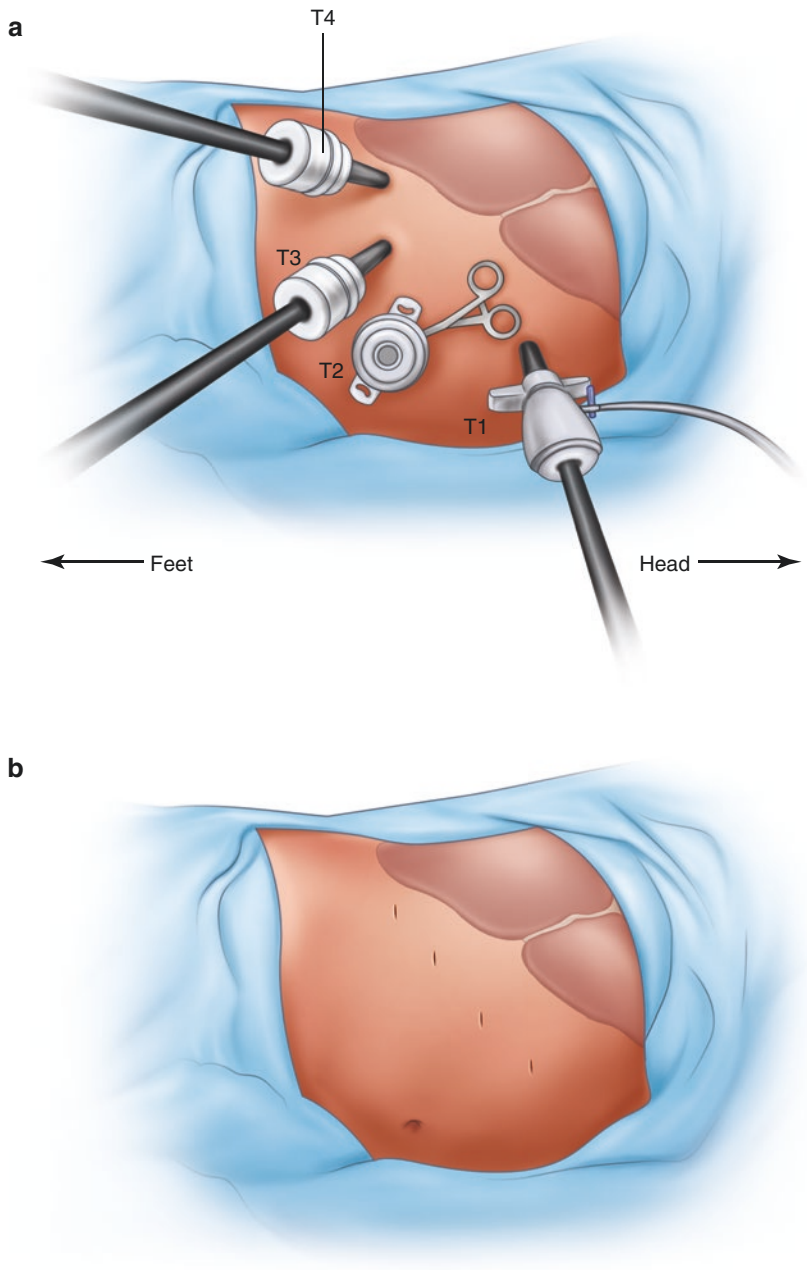


Figure 12.3

Dissecting the triangular ligament to mobilize the right liver

Figure 12.4

The apex of the adrenal gland's two limbs is dissected free, and the surgeon uses hook cautery to continue the dissection inferiorly

Figure 12.3

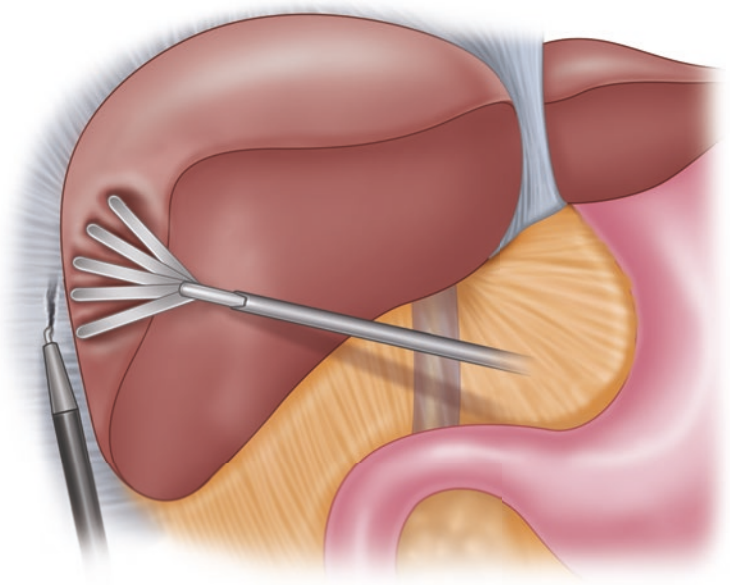


Figure 12.4

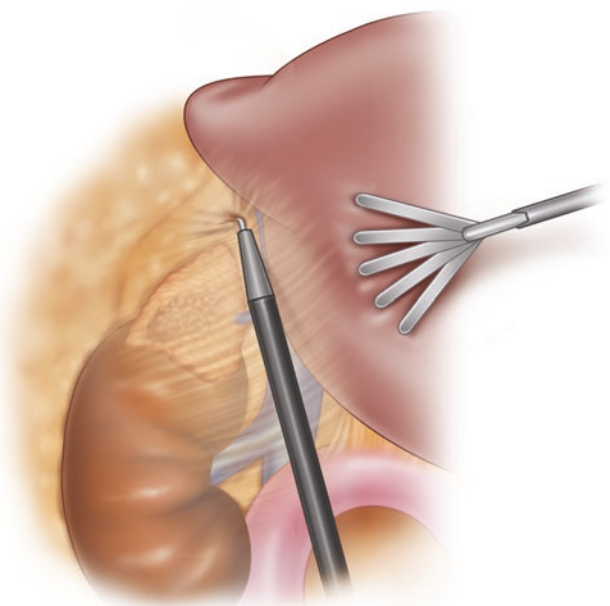


Figure 12.5

Identification, dissection, and ligation of the adrenal vein

Figure 12.6

Dissection of the inferior edge of the adrenal gland away from the renal vein and hilum

Figure 12.5

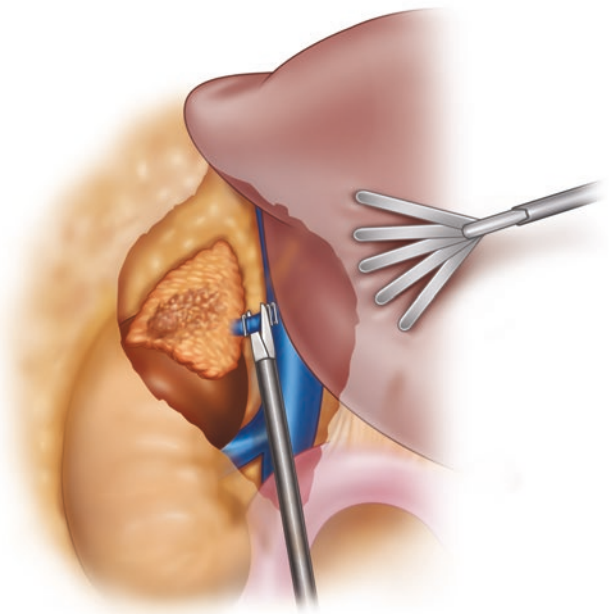


Figure 12.6

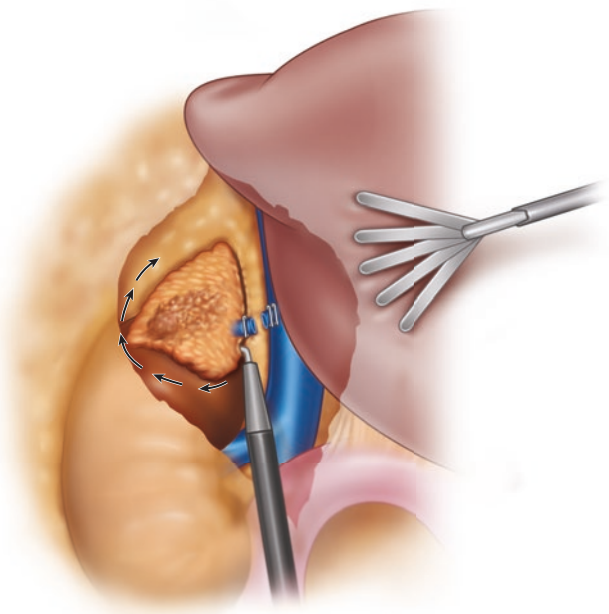


Figure 12.7

Separation of the periadrenal fat from the posterior muscle attachments

Figure 12.8

Removal of the specimen

Figure 12.7

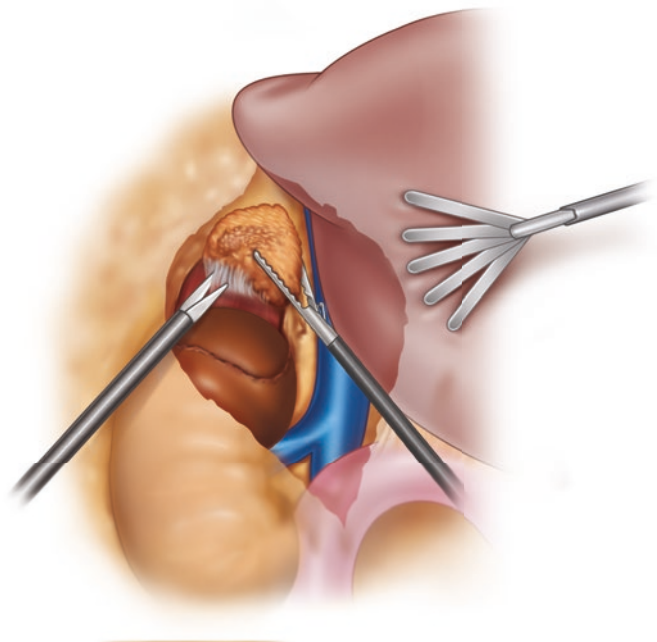
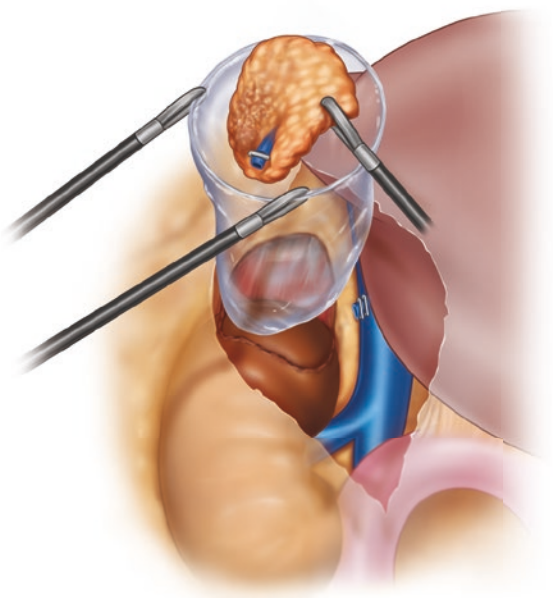


Figure 12.8



12.2.2 Laparoscopic Left Adrenalectomy

Similar to a laparoscopic right adrenalectomy, for a laparoscopic left adrenalectomy the patient is placed in a modified right lateral decubitus position (80° angle) with the aid of a beanbag (Fig. 12.9a). The patient is leaned slightly back to allow for better exposure to the anterior abdomen. An axillary roll is placed, and the bed is flexed to open the space between the costal margin and the iliac crest. Pillows are placed between the patient's legs, which are slightly bent to maintain a neutral position, and the patient is secured to the bed with 3-inch cloth tape across the knees, hips, and chest. The patient's left arm is laid on pillows or an arm board, and the patient's right arm is flexed at the elbow.

Figure 12.9

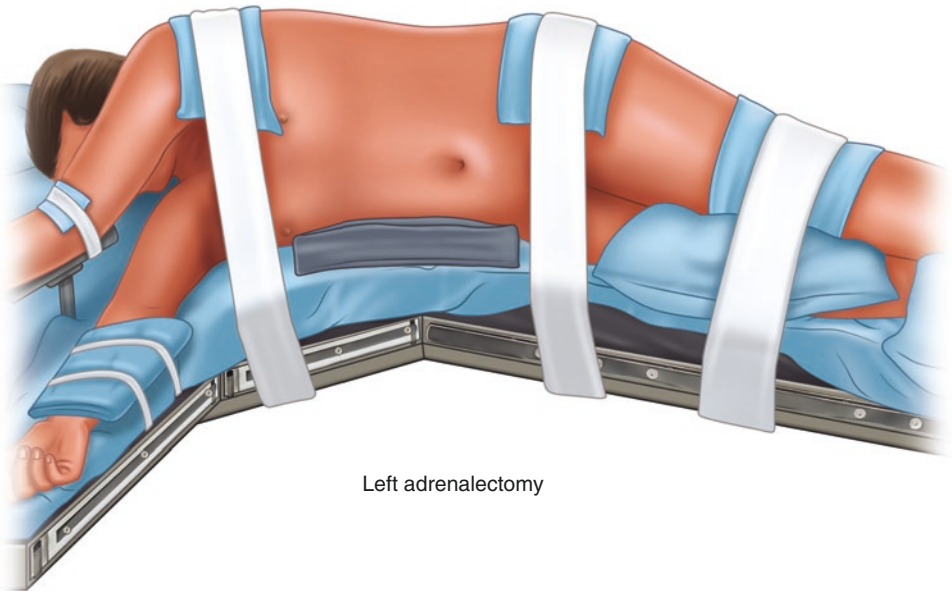
(**a**) Patient positioning for a laparoscopic left adrenalectomy. (**b**) Trocar sites for laparoscopic left adrenalectomy

Pneumoperitoneum is established using a Veress needle approximately 1–2 cm below the left subcostal margin in the midclavicular line (Palmer's point). The intra-abdominal pressure is initially bought to 20 mmHg and a 10-mm dilating trocar is placed (T1). Close communication with the anesthesiology team is paramount to look for a decrease in end-tidal CO_2, possibly indicating a CO_2 embolism. The pneumoperitoneum is then decreased to 15 mm Hg, and three additional 10-mm trocars are placed 1–2 cm below the left subcostal margin, evenly spaced between the midclavicular line and the anterior axillary line (T2–T4; Fig. 12.9b).

The first step in the operation is to release the splenic flexure of the colon (Fig. 12.10). This is done using hook cautery. The avascular attachments of the colon are demonstrated

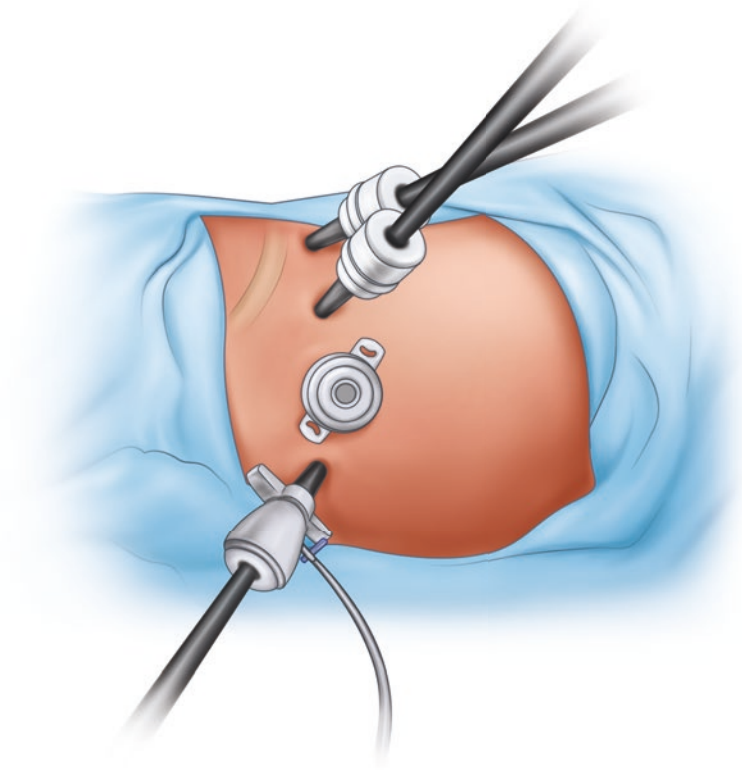
Figure 12.9

a



Left adrenalectomy

b



Port position

by retracting the colon inferiorly with an atraumatic laparoscopic grasper. Additional dissection may be necessary along the superior portion of the white line of Toldt to drop the colon away from the spleen.

A medial visceral rotation is then performed by dissecting the lateral attachments of the spleen off the lateral abdominal wall (Fig. 12.11). The dissection plane is between Gerota's fascia and the spleen and tail of the pancreas. A fan retractor can be used to gently retract the spleen and pancreas, allowing the surgeon to dissect the avascular attachments to the abdominal side wall and Gerota's fascia. This is a key step in the operation, and the surgeon must be mindful to stay in the plane anterior to Gerota's fascia instead of in the fascia or behind the kidney. As the spleen is rotated medially, the surgeon can identify the tail of the pancreas by its subtle yellow color, which is distinct from the surrounding retroperitoneal fat and the splenic vein running along its posterior edge. The dissection stops when the surgeon sees the fundus of the stomach at the cephalad limit of the dissection.

Once the spleen and pancreas are medially rotated, the valley between left crus of the diaphragm and medial limb of the adrenal gland is dissected from cephalad to caudad. As the dissection progresses along the medial edge of the adrenal, the inferior phrenic vein will be found running parallel to the dissection, toward the left renal vein (Fig. 12.12). The inferior phrenic vein is followed down to where it joins the left adrenal vein before it drains into the left renal vein.

Similar to the procedure for right adrenalectomy, the surgeon uses a hook cautery and straight laparoscopic grasper to dissect out the left adrenal vein (Fig. 12.13). Once the surgeon has adequate length on the vein, it can be clipped and divided. There are typically small arteries behind the vein, which must be cauterized.

The surgeon then uses hook cautery to dissect the inferior border of the adrenal gland off the renal hilum while avoiding a superior pole renal artery (Fig. 12.14). Once the kidney capsule is visible, it is safe to switch to a laparoscopic bipolar device for the remainder of the dissection.

As the adrenal gland is freed circumferentially from its attachments, it is also dissected free from the posterior musculature (Fig. 12.15). This plane is relatively avascular. It is important to be able to see the left crus of the diaphragm, the lateral abdominal musculature, and the psoas muscle posteriorly to make sure that all the adrenal and periadrenal tissue has been removed.

The specimen is then placed into a 4 × 6-inch nylon bag, which is introduced through the lateral port (T4). The open edge of the nylon bag is brought out through the port site; the skin is protected with towels. The adrenal gland and tumor are then morcellated and removed using ringed forceps,

Figure 12.10

Releasing the splenic flexure of the colon

under laparoscopic visualization to avoid damaging the spleen, kidney, or bowel (Fig. 12.16).

After removing the specimen, the lateral-most trocar is reinserted and the adrenal bed is examined for hemostasis. We do not routinely close the fascia of port sites created by dilating trocars. We do not leave a drain. The skin is closed with absorbable suture and glue.

12.3 Postoperative Management

In general, patients who undergo a laparoscopic adrenalectomy can be started on a regular diet and admitted to the ward. Patients with a pheochromocytoma are monitored in the postanesthesia care unit for 4 h. If they remain hemodynamically stable and do not require vasopressor support, then they can be sent to the ward; otherwise, they require admission to the intensive care unit. The Foley catheter is kept in place to accommodate postoperative diuresis; it is removed once the patient is ambulatory. Patients are typically discharged on the day after the operation.

After resection of a cortisol-secreting tumor or bilateral adrenalectomy, patients require corticosteroids in the perioperative period and should be managed in close consultation with an endocrinologist. For patients with an aldosterone-secreting tumor, blood pressure medications can be stopped, except for beta blockers, which can be continued at a reduced dosage. Supplemental potassium should be discontinued. A plasma aldosterone level is checked to confirm a cure. In patients with a pheochromocytoma, alpha-blocker medications should be discontinued. Electrolytes may be checked the day after surgery for patients with Cushing's and Conn's syndromes.

12.4 Complications

Complications following laparoscopic adrenal surgery are uncommon. Acute complications include postoperative hemorrhage, wound infection, and injury to adjacent organs such as the liver, kidney, diaphragm, and colon on the right side and the pancreas, spleen, kidney, diaphragm, and colon on the left side. Acute adrenal insufficiency may mimic sepsis, presenting with fever, nausea, vomiting, and hypotension. Diagnosis involves a cosyntropin stimulation test, but treatment is begun based on clinical suspicion, including correction of electrolyte abnormalities and administration of dexamethasone, which does not interfere with testing of cortisol levels [4]. Long-term complications include the development of abdominal wall hernias, which may be more common in patients with Cushing's syndrome.

Figure 12.10

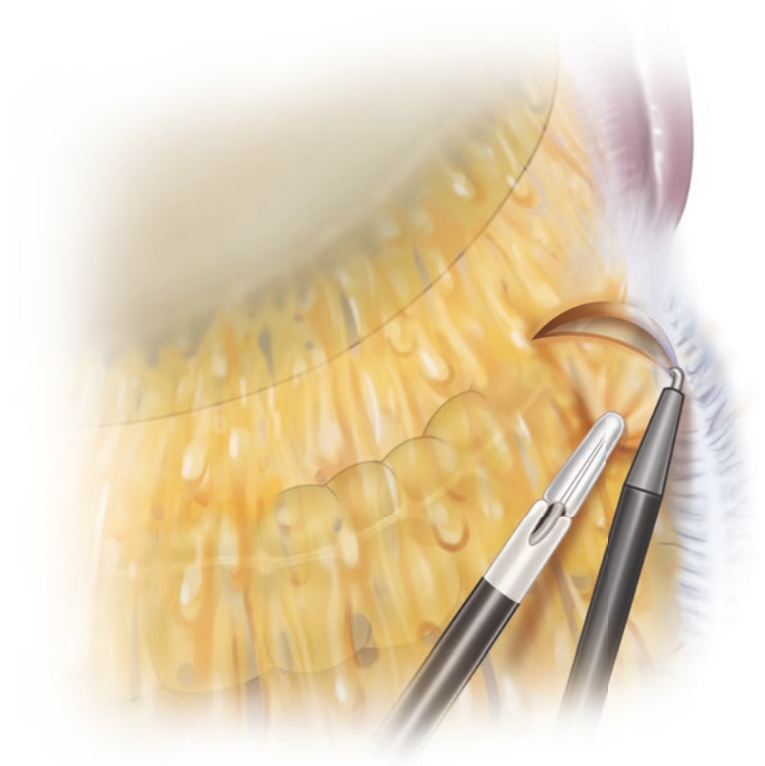


Figure 12.11

Medial visceral rotation is performed by dissecting the lateral attachments of the spleen off the lateral abdominal wall

Figure 12.12

During dissection along the medial edge of the adrenal, the inferior phrenic vein will be found running parallel to the dissection. The vein is followed down to where it joins the left adrenal vein

Figure 12.11

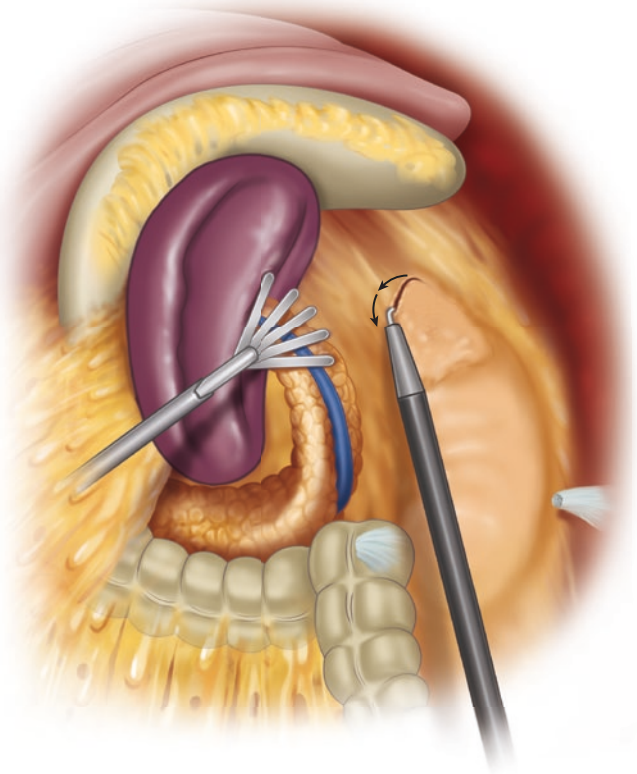


Figure 12.12

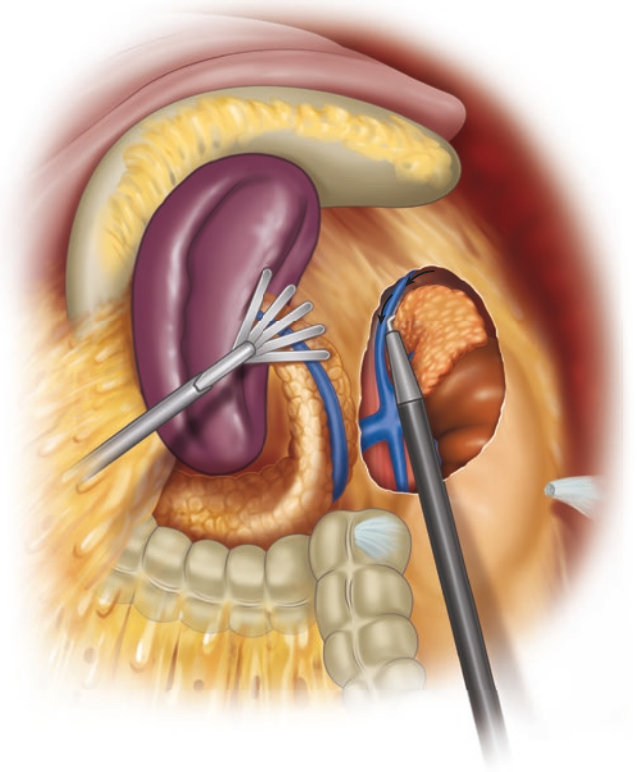


Figure 12.13

Dissection of the left adrenal vein

Figure 12.14

Dissection of the inferior border of the adrenal gland off the renal hilum, using hook cautery

Figure 12.13

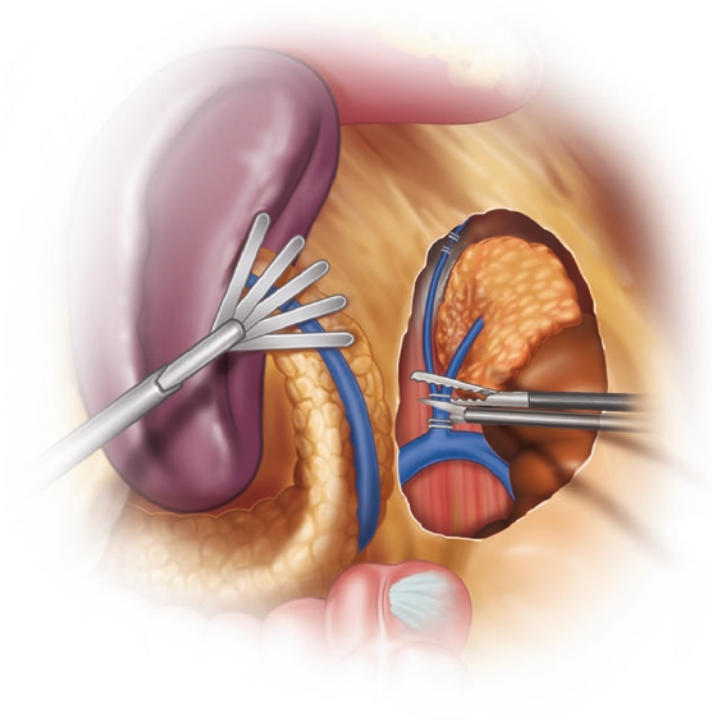


Figure 12.14

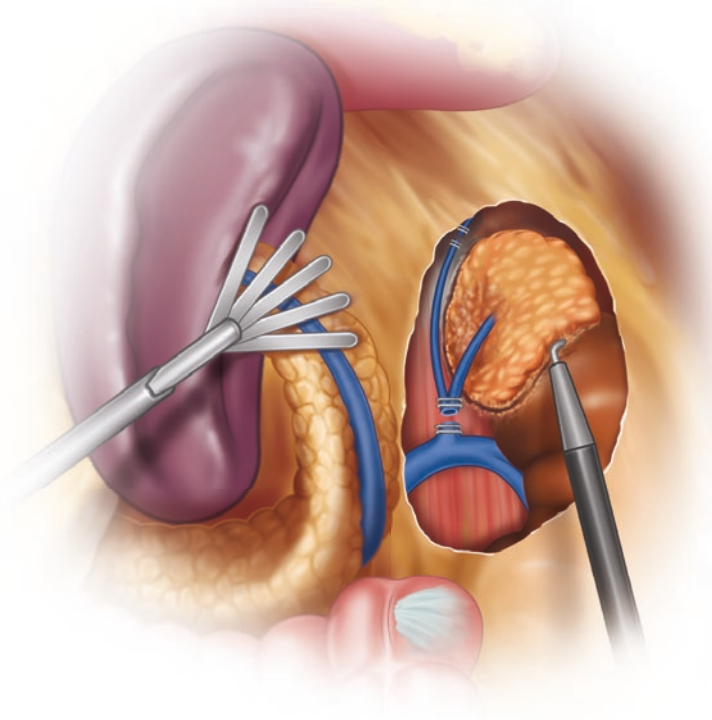


Figure 12.15

The adrenal gland is dissected free from the posterior musculature

Figure 12.16

Removal of the adrenal gland and tumor

Figure 12.15

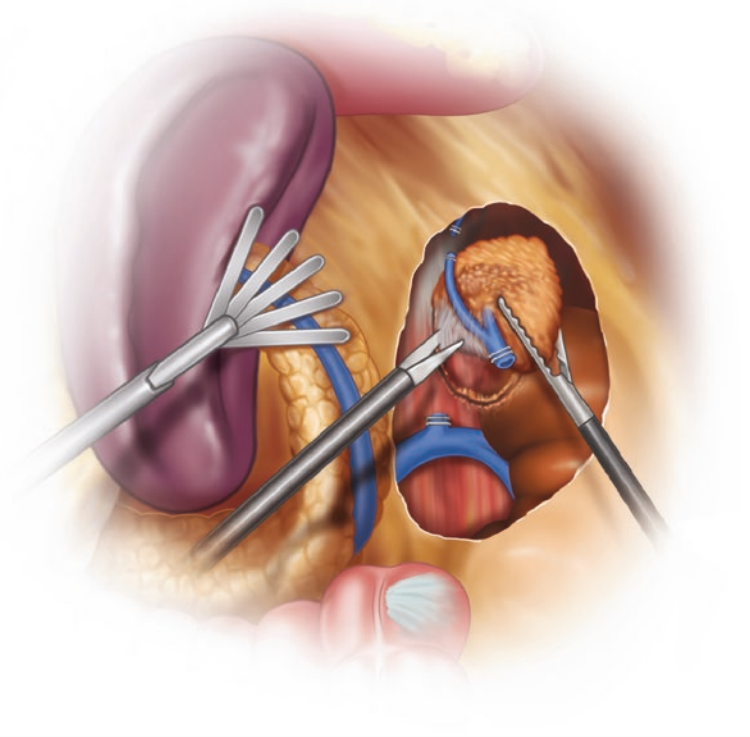
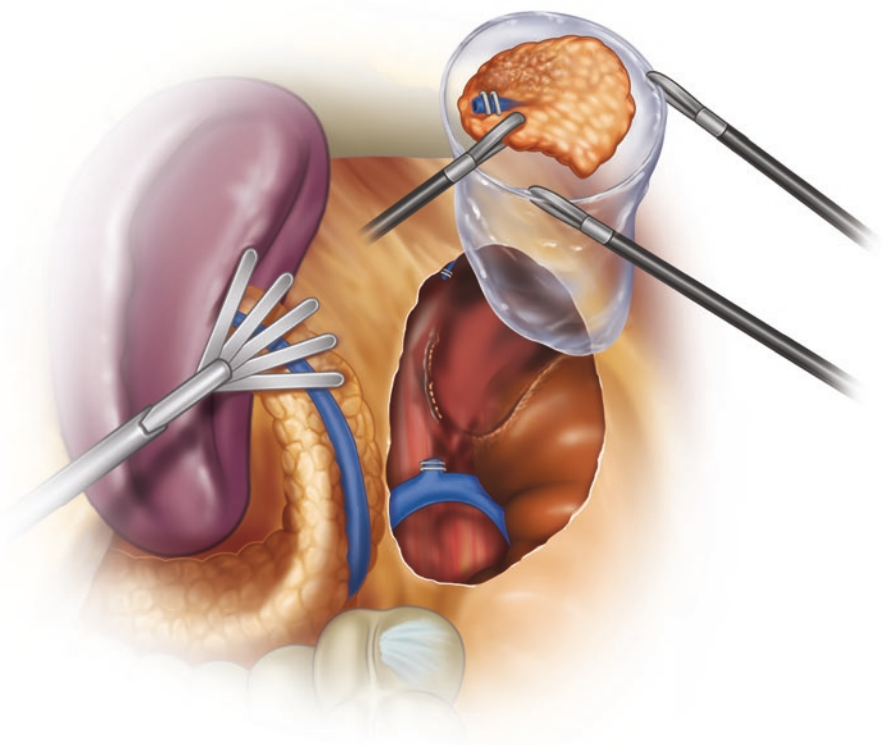


Figure 12.16



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Posterior Retroperitoneoscopic Adrenalectomy

13

Terry C. Lairmore

13.1 Introduction

Minimally invasive adrenalectomy is the surgical standard for the removal of most adrenal tumors. Benign adrenal neoplasms, whether functioning or nonfunctioning, are amenable to removal by laparoscopic techniques with very minimal morbidity and excellent outcomes. The laparoendoscopic posterior approach for adrenalectomy has rapidly grown in popularity in the United States in the past decade, following the initial reports of the simplicity of this approach, as well as excellent outcomes in Europe [1]. More recently, modifications to established procedures have resulted in novel surgical techniques for adrenalectomy, including the application of robotic systems to this approach. Future advances in technology should result in the continued evolution of techniques and refinement of surgical capabilities, with the ultimate goals of enhanced surgeon proficiency and possibly improved patient outcomes.

Laparoscopic adrenalectomy was initially described in 1992 [2]. The first such operations were performed with a transperitoneal approach, using conventional laparoscopic techniques. Early reports confirmed excellent outcomes with laparoscopic/endoscopic removal of selected adrenal neoplasms. Subsequently, other groups reported the results of a lateral or posterior retroperitoneal approach to adrenalectomy. Compared with open adrenalectomy, laparoscopic adrenalectomy results in reduced postoperative pain, less blood loss, decreased wound complication rate, shorter hospital stay, and shortened patient convalescence.

Adrenalectomy through a posterior laparoendoscopic approach has been utilized with increasing frequency in the United States in recent years. Compared with transperitoneal laparoscopic adrenalectomy (TLA), the potential advantages of posterior retroperitoneoscopic adrenalectomy (PRA) include a more direct anatomic approach (obviating the need to mobilize overlying anatomic structures), shorter operative times, and reduced risk of sequelae from entering the peritoneal cavity, such as inadvertent bowel injury or postoperative formation of intra-abdominal adhesions. This approach has advantages for patients who have had multiple prior anterior peritoneal operations, as well as patients with bilateral adrenal pathology. Some potential disadvantages of the approach include surgeon unfamiliarity with a posterior anatomic view, and the risk of complications related to the use of increased insufflation pressures, including possible deleterious intraoperative cardiovascular effects, pneumothorax or pneumomediastinum, or extensive subcutaneous emphysema. Available reports confirm excellent and generally comparable outcomes with both TLA and PRA. Further studies may associate marginal or significant advantages with one of these approaches, but currently there are no evidence-based studies to support such advantages.

13.2 Surgical Technique

The sections below provide a stepwise description of a surgical technique for posterior endoscopic (retroperitoneoscopic) adrenalectomy.

13.2.1 Patient Positioning and Trocar Placement

After induction of general anesthesia and endotracheal intubation, a urinary catheter and appropriate hemodynamic monitoring are instituted. An arterial line and central venous catheter should be placed for patients with hormonally active tumors. A general overview of a suggested physical organization for the operating room equipment and personnel is depicted in Fig. 13.1. The patient is then rotated into the prone position with knees and hips flexed at 90° (Fig. 13.2). The positioning can be facilitated by the utilization of a

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J.R. Howe (ed.), *Endocrine and Neuroendocrine Surgery*, Springer Surgery Atlas Series, DOI 10.1007/978-3-662-54067-1_13

specialized padded pillow for prone patient positioning, such as the Cloward surgical saddle (NL999, Cloward Instruments, Honolulu, HI). The iliac crests are optimally aligned on the lateral rises of the surgical cushion, allowing the patient's abdominal viscera to fall anteriorly and providing maximum reduction of the lumbar lordosis. This positioning optimizes exposure and facilitates access to the posterior subcostal space. With the patient prone, a brief preoperative ultrasound examination can be used to precisely localize the kidney and its upper pole, and thus the expected position of the surgical target, the adrenal gland. This maneuver can be helpful to optimize the placement of the trocar incisions and individualize access depending on variations in body habitus.

Initial trocar placement and access to the operative space is begun by making a transverse incision approximately 1.5 cm in length, below the tip of the 12th rib (Fig. 13.3). The retroperitoneal space is entered by sharp dissection through the thoracolumbar fascia and the erector spinae and quadratus lumborum

Figure 13.1

Organization of the operating room equipment and personnel for posterior retroperitoneoscopic adrenalectomy

muscles. Gentle digital exploration confirms appropriate entry into the retroperitoneal fat, which readily yields way. The smooth inner surface of the posterior parietal wall can be felt with minimal blunt exploration of the finger in this potential space. In general, extensive finger dissection is not necessary to create the appropriate working space, which develops readily with the subsequent pressures following gas insufflation. It is important to avoid creating a false plane between the muscular layers or soft tissue of the posterior lumbar area, which can result in difficulty maintaining the appropriate pressures during the procedure, or the development of extensive subcutaneous emphysema. Next, two additional medial and lateral incisions are made, with a minimum optimal separation of 5 cm, and two 5-mm trocars are placed into the retroperitoneal working space with direct digital guidance (Fig. 13.4). A 12-mm blunt trocar (#OMS-T12BT, AutoSuture/Covidien, Mansfield, MA) with an anchoring inflatable balloon and adjustable sleeve is placed in the center port access site.

Figure 13.1

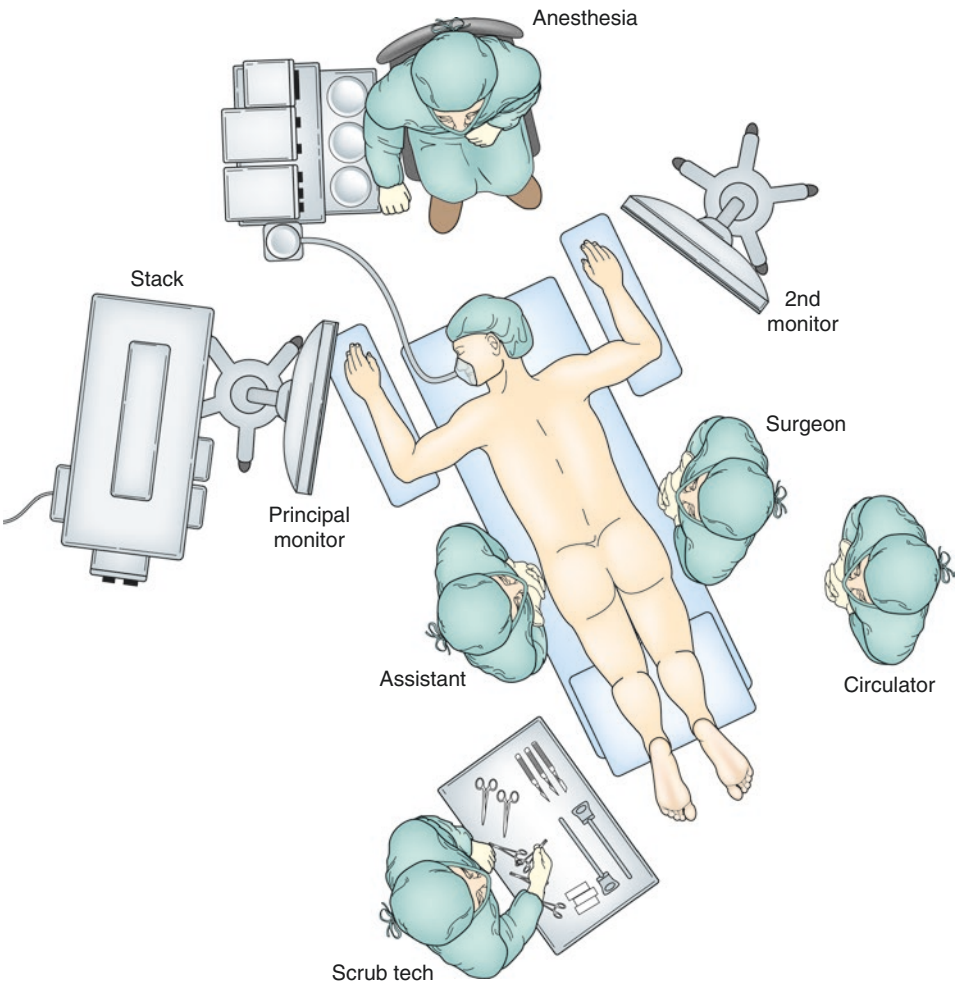


Figure 13.2

Positioning of the patient

Figure 13.3

The initial incision for 12 mm port (middle), with additional 5 mm port sites (medial and lateral)

Figure 13.2

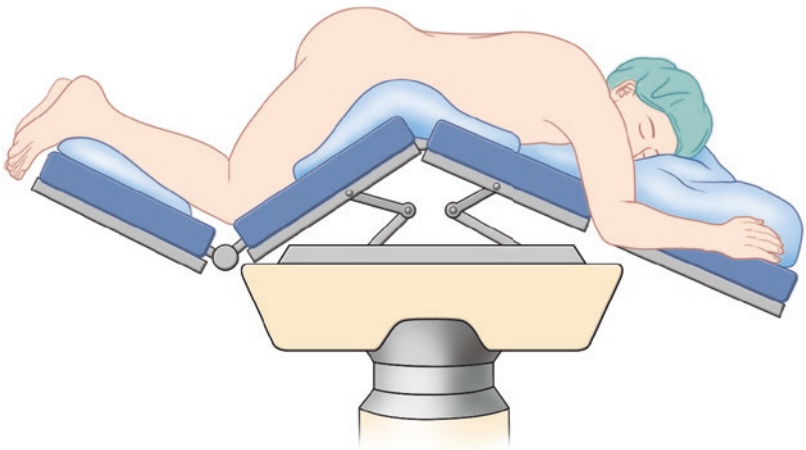


Figure 13.3

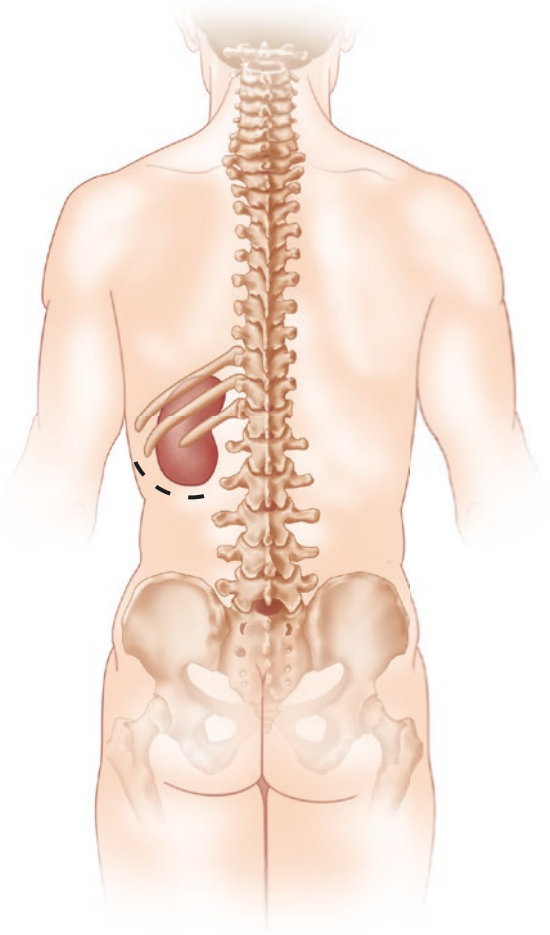
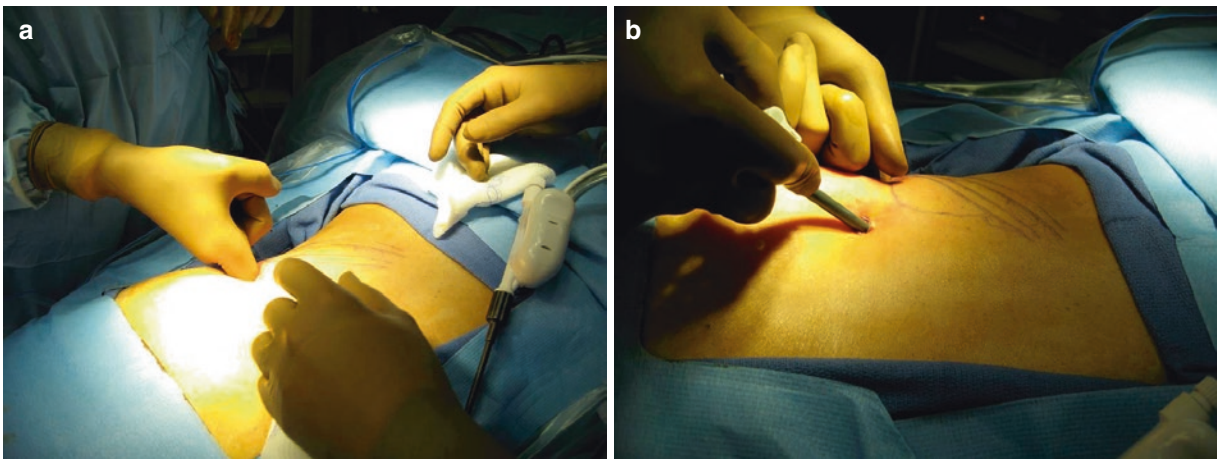


Figure 13.4

(**a**) The 12 mm trocar site incision is made in the left flank, and blunt dissection performed with a finger to enter the retroperitoneal space. (**b**) The medial 5 mm trocar is placed into the retroperitoneal working space with digital guidance

Figure 13.4



13.2.2 Creation of Working Space and Identification of Critical Landmarks

Insufflation pressures of 18–24 mmHg are utilized in the retroperitoneum to create an adequate working space. Opening of this potential space requires only the institution of positive gas insufflation and some gentle spreading with blunt-tipped instruments. A gentle, opposing, spreading motion of two instruments is used to open Gerota's fascia (Fig. 13.5), exposing the perirenal and periadrenal fat. The upper pole of the kidney should be identified as a critical starting landmark for the dissection. The adrenal gland is found superomedial

Figure 13.5

The opening of Gerota's fascia, exposing the perirenal and periadrenal fat

Figure 13.6

The surgical anatomy of the adrenal glands from the posterior view

to the upper renal pole, and is generally situated very medially against the paraspinous muscles. The inferior portion of the gland occasionally extends in part somewhat anterior to the kidney (behind the kidney as viewed from the posterior approach). The surgical anatomy of the adrenal glands from the posterior view is shown in Fig. 13.6. The amount of retroperitoneal fat depends on the patient's body habitus, and initial identification of the superior pole of the kidney is the key to establishing the surgical anatomy required to continue the dissection.

Figure 13.5

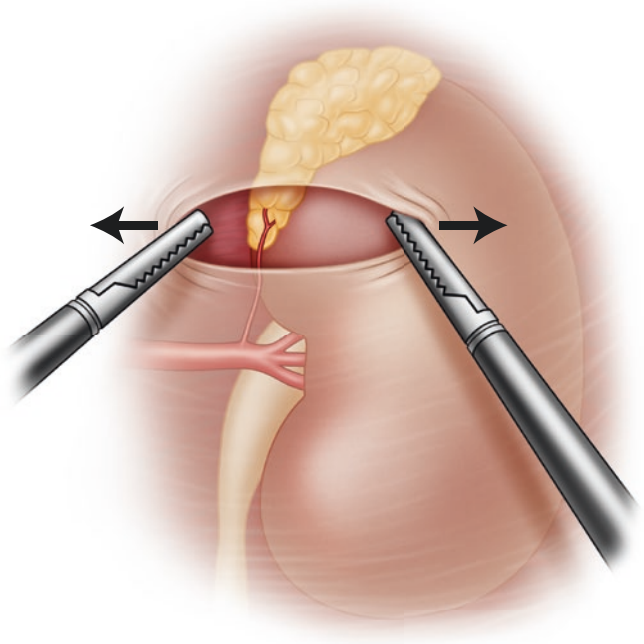
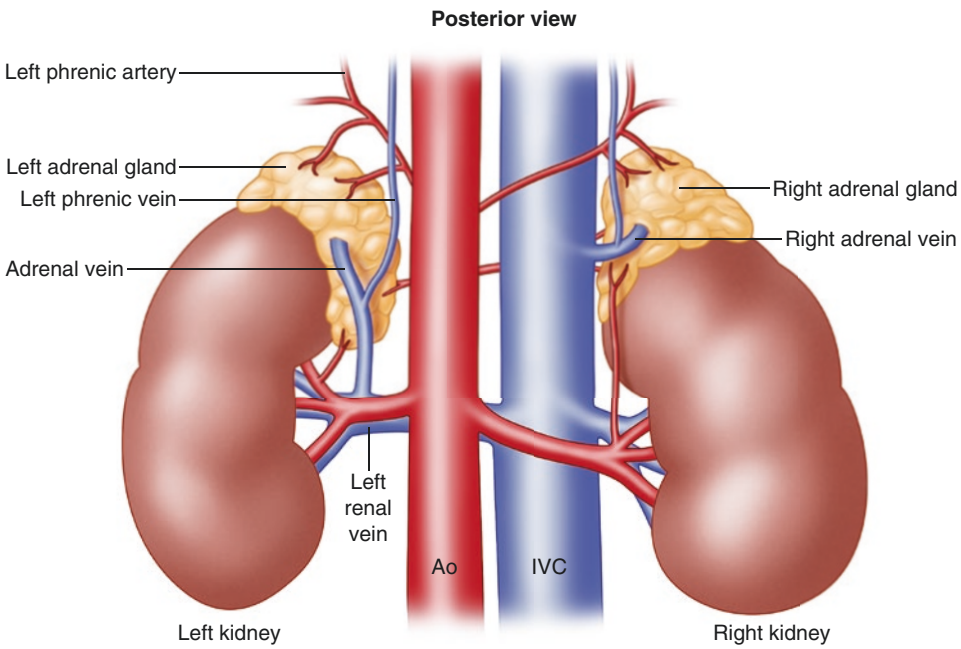


Figure 13.6



13.2.3 Adrenal Gland Dissection: Operative Strategy

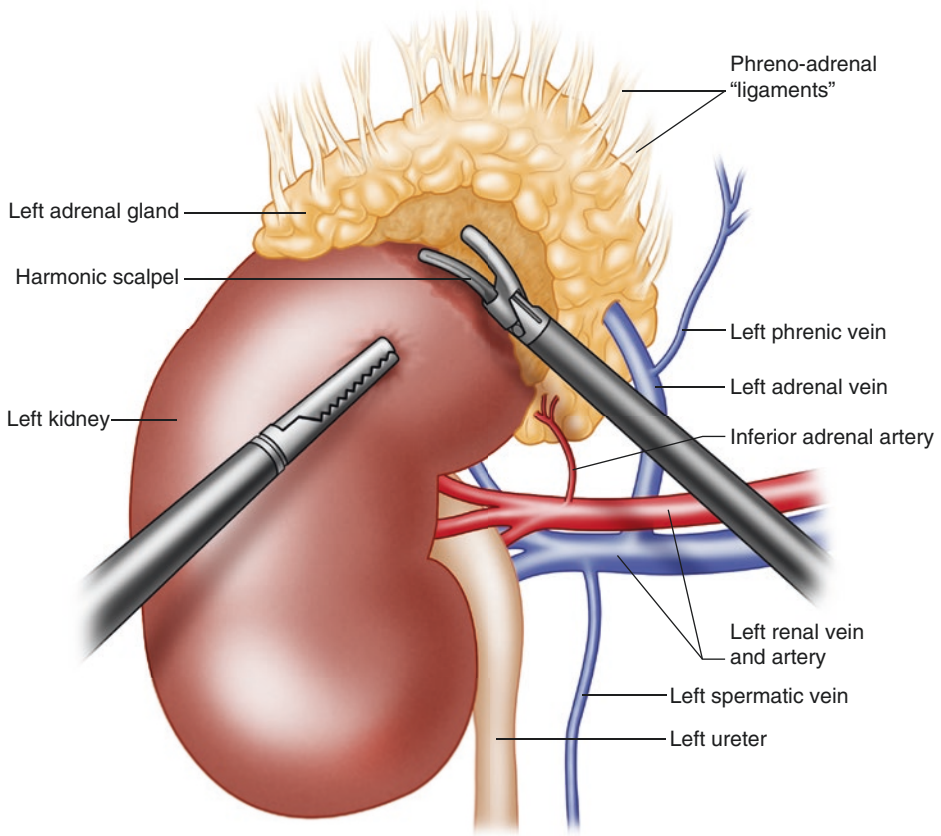
The initial localization of the adrenal gland within the retroperitoneal fat may be elusive at first, but with experience, the bright yellow appearance of the adrenal cortex is readily identified. Ultrasound may facilitate the expedient localization of the gland and may be performed in the operating room after patient positioning and prior to the incision, or with a laparoendoscopic ultrasound transducer. A suggested strategy for adrenal

Figure 13.7

The upper pole of the kidney is gently retracted laterally and inferiorly, and the inferior and medial border of the left adrenal gland is dissected

gland dissection is to initially develop the plane between the upper border of the kidney and the inferior edge of the adrenal gland. After defining the adrenal gland border, this dissection is continued around the inferior and medial aspects of the gland until the adrenal vein is identified. The upper pole of the kidney is gently retracted laterally and inferiorly, and the inferior and medial border of the adrenal gland is dissected (Fig. 13.7). The superolateral (diaphragmatic) and anterior (peritoneal) attachments of the adrenal gland are left intact until later, leaving the gland anchored for optimal dissection.

Figure 13.7



13.2.4 Identification and Division of the Adrenal Vein

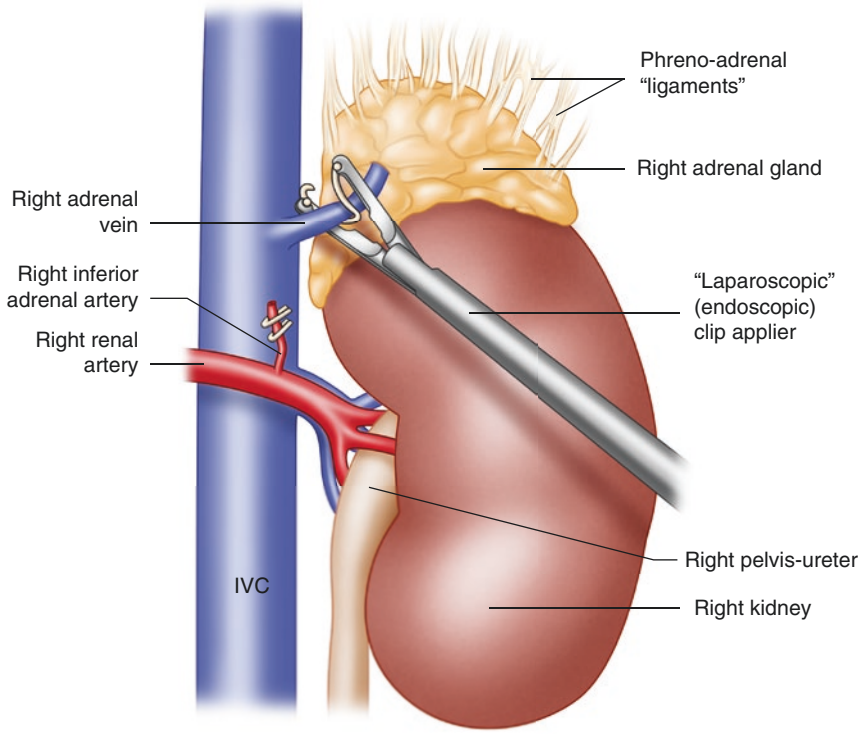
The adrenal vein is identified early and divided. The adrenal vein anatomy can vary, especially on the right. The left adrenal vein arises from the renal vein, and a smaller phrenic vein branch coursing superiorly and medially is very constant. On the right, the adrenal vein arises directly from the inferior vena cava; it generally originates somewhat posteriorly on the vein and takes a more horizontal course. Anatomic variations in the venous drainage can occur on the left and are somewhat more frequent on the right. An ultrasonic energy device (harmonic scalpel) can be helpful in dividing small arterial branches when dissecting the periadrenal fat. A

Figure 13.8

After dissection, the right adrenal vein is divided between surgical clips. *IVC* Inferior vena cava

curved or right-angled dissecting instrument can be used to completely define the adrenal vein and separate it from the loose investing connective tissue. The adrenal vein represents the single important vascular structure to be controlled during adrenalectomy, and it is recommended that this critical structure be identified and addressed early in the operative procedure. After it is safely dissected, the adrenal vein is divided between surgical clips (Fig. 13.8). Using gentle blunt retraction of the adrenal gland, the remaining periadrenal fat and soft tissue attachments are divided using an advanced laparoendoscopic energy device to complete the dissection. The adrenal gland is removed in a specimen bag.

Figure 13.8



13.3 Robot-Assisted Retroperitoneoscopic Adrenalectomy (RAPRA)

The challenges of the posterior endoscopic approach include a smaller working space, limitations related to the rigid design of conventional instruments, and the need to position port sites close together, resulting in the potential for instrument conflicts and difficult operating angles. The application of robotic techniques to laparoendoscopic adrenalectomy follows the logical progression of laparoscopic technology and novel instrumentation.

Robotic surgical systems provide several advantages:

- Improved three-dimensional visualization and magnification of the operative field
- Articulating instrumentation with improved ability to work within a smaller physical space
- Optimized surgeon ergonomics
- Tremor filtering
- Motion scaling

Robotic surgery also has some potential disadvantages:

- Markedly more complex instrumentation and setup requirements
- The need for a specialized operative support team
- Increased costs
- Increased total operative time
- A lack of evidence-based data for equivalent or superior patient outcomes and patient acceptance

Initial reports of robot-assisted techniques have confirmed the feasibility and safety of this modification of laparoscopic adrenalectomy and have demonstrated expected excellent surgical outcomes, comparable to outcomes for conventional laparoscopic adrenalectomy [3–5]. It is also important to consider costs and investment in setup time, as well as the need for a specialized surgical suite and team. The fixed costs of initial capital expense and of disposable equipment and the need for a specialized surgical suite and team may be justified if operative times are significantly decreased with further experience. Further analysis of surgical results and patient outcomes will be necessary to define the role of robot-assisted adrenalectomy.

13.4 Results and Conclusions

A minimally invasive operation is the preferred surgical technique for removal of small, functioning or nonfunctioning adrenal neoplasms. The adrenal gland may be accessed anatomically from an anterior transperitoneal approach (TLA) or from a posterior retroperitoneal approach directly through the back. Minimally invasive PRA involves a more direct anatomic approach and generally fewer port sites. It offers operative simplicity in patients with bilateral tumors or multiple previous anterior operations. In general, PRA does not require advanced suturing techniques; the single major vascular structure to be identified and divided is the adrenal vein. A few important challenges associated with the posterior approach include the small working space and limited operative angles for dissection or application of surgical clips when working with rigid laparoendoscopic instruments, but the addition of robotic articulating instrumentation may provide significant ergonomic advantages in the very small working space. Another potential advantage of robotic surgery is its enhanced precision in identifying and dividing the adrenal vein and dissecting the adrenal gland, as a result of magnification and improved three-dimensional visualization.

The stepwise technique for posterior endoscopic removal of the adrenal gland described in this chapter is associated with expected excellent outcomes and very low morbidity. The application of robotic systems technology is a further modification that may provide advantages over this approach and further refinement of the technique [3–5]. Additional advances such as robotic adaptations of single incision laparoscopic surgery (SILS) represent future areas for study. Currently, there is no evidenced-based confirmation of improved results or outcomes in patients undergoing minimally invasive adrenalectomy via the posterior endoscopic approach, when compared with conventional transperitoneal laparoscopic adrenalectomy. Continued refinements in minimally invasive technology are almost certain to occur, however. Technologic advances in minimally invasive techniques will continue to result in modifications to minimally invasive adrenalectomy and expanded surgical experience and indications.

Acknowledgments The author wishes to acknowledge John C. Hendricks, MD, for the original drawings that were created for this work and redrawn here, as well as the invaluable technical advice and assistance of Patrick S. Lowry, MD; Kristofer R. Wagner, MD; Aaron T. Ludwig, MD; and Samuel K. Snyder, MD.

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Part IV

Stomach and Duodenum

Surgery for Duodenal and Gastric Neuroendocrine Tumors

14

Jeffrey A. Norton

14.1 Duodenal Neuroendocrine Tumors

14.1.1 Introduction

Duodenal neuroendocrine tumors (NETs) (also called carcinoid tumors) are rare, with an incidence in the population of approximately 1 per million. They may be found incidentally on endoscopy as a mass in the submucosa at endoscopy (Fig. 14.1), or they can produce hormones that cause clinical syndromes. These tumors can make somatostatin, vasoactive intestinal polypeptide (VIP), or more commonly, gastrin. When they make gastrin, it is called the Zollinger-Ellison syndrome (ZES). Duodenal NETs may be either benign or malignant, but even when malignant, they have a low malignant potential. In general, they have an excellent prognosis.

Patients with somatostatinomas commonly have type 2 diabetes and steatorrhea. Somatostatinoma is diagnosed by measuring elevated fasting serum levels of somatostatin. VIPomas present with severe secretory diarrhea and marked electrolyte abnormalities that include hypokalemia, hypochloremia, and hypercalcemia; they are diagnosed by measuring fasting levels of VIP. ZES typically presents with severe peptic ulcer disease, diarrhea, and/or gastroesophageal reflux disease. The diagnosis is made biochemically by measuring increased fasting serum levels of gastrin (>100 pg/mL), increased basal acid output (>10 mEq/L, or >5 mEq/L in patients with prior acid-reduction surgery or a gastric pH <2), and an abnormal secretin test (increase of >200 pg/mL in serum gastrin concentration after 2 U/kg of intravenous secretin). Although gastrinomas can arise in the pancreas, two thirds arise in the wall of the duodenum. Duodenal NETs can occur sporadically (nonfamilial) or as part of multiple endocrine neoplasia type 1 (MEN1). Patients with duodenal NETs and MEN1 usually have multiple duodenal tumors and may have concomitant multiple pancreatic NETs, primary hyperparathyroidism, or both.

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14.1.2 Surgery

Patients who have ZES with localized, completely resectable tumors or those that cannot be identified by imaging are candidates for surgery. Patients who are referred with biopsy-proven duodenal NET are also candidates. Pernicious anemia and achlorhydria must be excluded, as they may represent an increased serum level of gastrin secondary to a lack of stomach acid (as discussed below regarding Type 1 gastric NETs). Similarly, medications that inhibit acid production (e.g., H_2 receptor antagonists, proton pump inhibitors [PPIs]) will cause elevated levels of gastrin. Preoperative localization studies include CT or MR imaging of the pancreas and duodenum, as well as the liver, to exclude liver metastases. Somatostatin receptor scintigraphy (SRS; Octreoscan) is the single best imaging study. It images 90% of gastrinomas, and because it is a whole-body scan, it can detect distant metastases. It may miss small duodenal gastrinomas, however. A new type of nuclear medicine scan that appears to be more sensitive is ^{68}Ga-DOTA-PET. Endoscopic ultrasound also may detect small duodenal tumors and lymph node metastases. Patients with ZES should be placed on PPIs to control acid hypersecretion. The usual dose of pantoprazole (Protonix) is 80 mg PO or IV twice daily. Patients with MEN1 and their families may have associated endocrinopathies, primary hyperparathyroidism, nephrolithiasis, prolactinoma, insulinoma, Cushing's syndrome, NETs, and/or carcinoid syndrome. Clinical evaluation should exclude these conditions, especially primary hyperparathyroidism, which requires parathyroid surgery (usually removal of three and one half parathyroid glands) prior to the duodenal procedure.

Opening the abdomen and general exploration is commonly performed through a bilateral subcostal incision focused more on the right side of the abdomen than the left.

J.R. Howe (ed.), *Endocrine and Neuroendocrine Surgery*, Springer Surgery Atlas Series, DOI 10.1007/978-3-662-54067-1_14

Duodenal NETs are often small (less than 1 cm). Consequently, these tumors are commonly missed on preoperative imaging and intraoperative dissection. Transillumination of the duodenum may be helpful. The tumor appears as an opaque mass within the wall (Fig. 14.2a). Opening the duodenum for transmural palpation is another method for operative detection. A Kocher maneuver is performed to mobilize the duodenum. We generally try to open the duodenum longitudinally and close transversely, so as not to narrow the lumen (Fig. 14.2b). If the tumor is diagnosed serendipitously by endoscopy before surgery, often the gastroenterologist will inject blue dye to mark the precise location of the tumor in the duodenum. Finally, during the initial exploration, the liver is also carefully evaluated for metastases by mobilization, palpation, and intraoperative ultrasound.

The next step involves mobilizing the entire right colon and hepatic flexure away from the duodenum, allowing better palpation of the duodenum. Duodenal NETs feel like small, firm nodules within the wall. They are usually mobile and feel like a pea. If the location of the tumor is not known, a duodenotomy (opening the duodenum) is essential because it is often the only way to visualize and palpate small duodenal NETs. This duodenal incision is used to explore the entire duodenum. The tumor originates in the submucosa and commonly dimples the mucosa. The surgeon can palpate the tumor within the wall of the duodenum with the index finger in the lumen and the thumb on the outside (Fig. 14.2b). Because the neoplasm arises from the submucosa and usually invades the mucosa, it cannot be effectively removed endoscopically and requires full-thickness excision with a rim of normal duodenum around the tumor.

In patients with MEN1, multiple duodenal NETs may be present, and the surgeon must carefully palpate and inspect the remainder of the inner surface of the duodenum to identify other neoplasms and plan a complete excision of all NETs. If the NETs are multiple and more extensive, or if it involves the ampulla of Vater and is larger than 2 cm, it may be more malignant and require a wider, more effective excision such as a pancreaticoduodenectomy (Whipple procedure). Do not confuse the ampulla of Vater or the entrance of the minor pancreatic duct with an NET. When uncertain, identification of the orifices of the pancreatic duct can be aided by the intravenous administration of secretin, which elicits pancreatic exocrine secretion. A cholangiocatheter placed through the cystic duct into the common bile duct and into the duodenum will also help to identify the ampulla.

After excising a duodenal gastrinoma, the duodenum is closed with a double-layer suture of full-thickness monofilament absorbable suture (e.g., PDS) and reinforced with a seromuscular layer of interrupted silk suture. In general, it is

Figure 14.1

Duodenal NET identified incidentally during endoscopy. Note the tumor originates in the submucosa and is seen as a small mass within the duodenal wall

always closed in a transverse direction, so as not to narrow the lumen (Fig. 14.2b). If a long duodenotomy is necessary, a longitudinal closure may be performed, but it may narrow the duodenum, causing obstruction. For bulky tumors in the pancreatic head, tumors involving the pancreatic duct, or duodenal tumors involving the ampulla of Vater, a pylorus-preserving pancreaticoduodenectomy may be necessary.

Following local excision of duodenal NETs, all lymph nodes within the region are excised in a systematic fashion starting with the hepatoduodenal ligament, the porta hepatis, and both the anterior and posterior border of the head of the pancreas (Fig. 14.3). The lymph node dissection is done after performing an extended Kocher maneuver in which the duodenum and the head of the pancreas are widely mobilized, as well as mobilization of the ascending colon, hepatic flexure, and transverse colon away from the head of the pancreas. This mobility of the duodenum and the pancreatic head allows dissection of all lymph nodes from both the anterior and posterior surface of the head of the pancreas. We have found that the harmonic scalpel facilitates bloodless lymph node excision. Quite commonly, the surgeon can find approximately five nodes embedded in the anterior head of the pancreas. The posterior nodes may be associated with enlarged lymph nodes between the inferior vena cava and the aorta, in the area of the left renal vein. These nodes should be excised as well. One can typically obtain five lymph nodes from the area posterior to the head of the pancreas and anterior to the vena cava. For the portal lymph node dissection, we identify and protect the common hepatic artery, the common bile duct, and the portal vein. We dissect lymph nodes around the origin of the common hepatic artery, along the right side of the common bile duct and underneath the duct close to the portal vein. Usually, about five nodes can be removed from the porta hepatis by dissecting along these structures. Complete pancreatic head, caval, and portal lymph node dissection is important because the tumors commonly spread to these lymph nodes. Detection of lymph node metastases suggests that the NET is malignant and portends a poorer prognosis.

The patient with ZES is kept on the same dose of PPI postoperatively for 3–6 months because parietal cell hypertrophy occurs, and acid hypersecretion decreases slowly. For ZES, a postoperative fasting serum gastrin measurement should be compared to the preoperative level. We typically wait 6 months before once again measuring all the tests—fasting serum gastrin, basal acid output, and secretin-stimulated gastrin—to diagnose ZES.

Postoperative complications include duodenal leak, bleeding, and pancreatitis. Duodenal stricture and tumor recurrence may be seen on long-term follow-up.

Figure 14.1

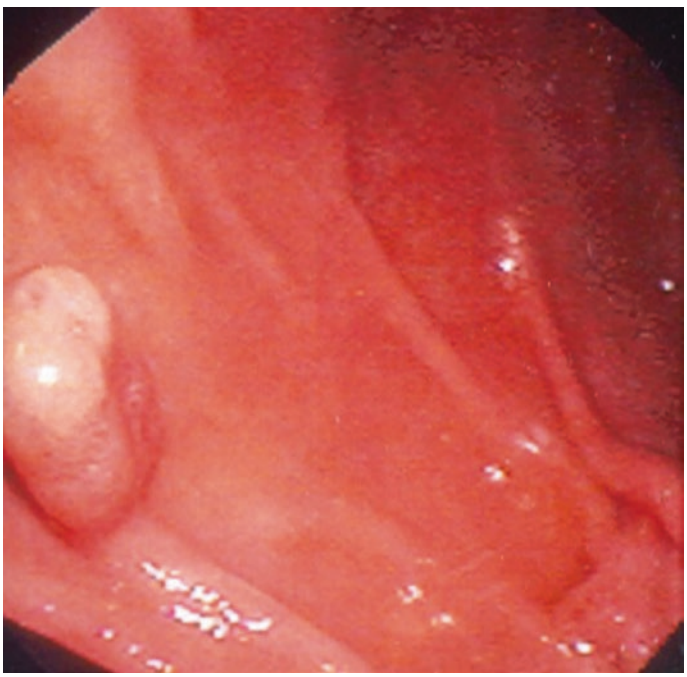


Figure 14.2

Duodenal neuroendocrine tumors: operative strategy. (**a**) Duodenal transillumination may show the tumor as an opaque mass (*arrow*). Duodenotomy allows better palpation. (**b**) Transillumination of the duodenum shows an NET as an opaque mass within the wall. After duodenotomy, the duodenum is usually closed transversely to avoid narrowing the lumen

Figure 14.3

Systematic lymph node excision for duodenal NETs

Figure 14.2

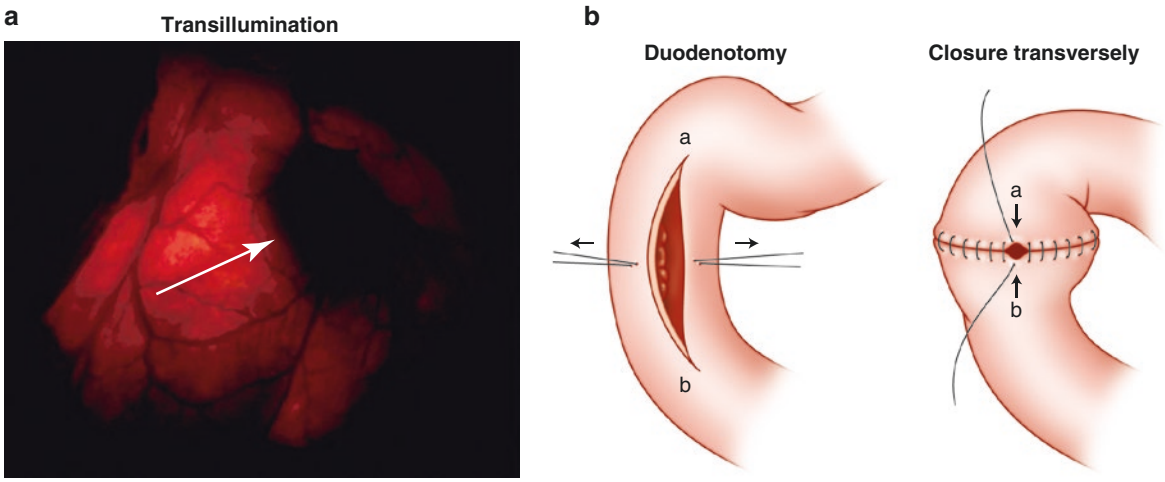
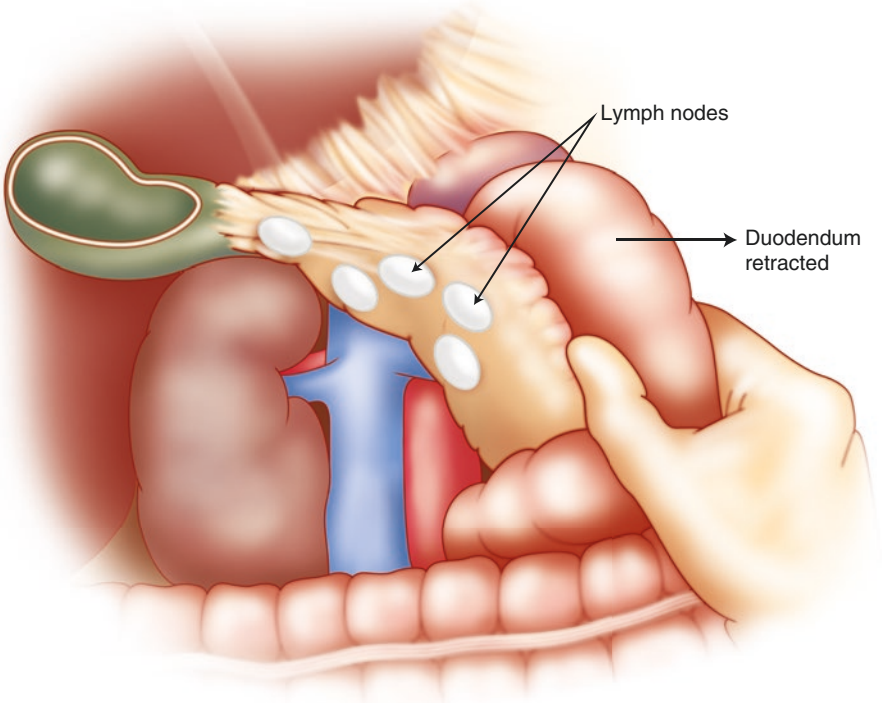


Figure 14.3



14.2 Gastric Neuroendocrine Tumors (Carcinoid Tumors)

14.2.1 Introduction

Gastric NETs can be broadly categorized into well-differentiated and poorly-differentiated. These tumors are divided into those arising from enterochromaffin cell hyperplasia due to excess gastrin stimulation (types I and II) and sporadic tumors (type III), which may be well or poorly-differentiated. There has been an increase in the incidence of gastric NETs, accounting for approximately 1.8% of gastric malignancies, compared with 0.3% previously. Age-adjusted incidence rates also have shown a marked increase in incidence, especially in white women. This increase is related to an increased incidence of chronic atrophic gastritis among females, increased use of PPIs, and increased endoscopy with improved detection. The mean age at diagnosis is 65 years. Of gastric NETs, 70–80% are type I, and 64.5% of these occur in women (Fig. 14.4a, b). These tumors arise in patients with chronic atrophic gastritis in which the increase in gastric pH causes gastrin hypersecretion and enterochromaffin-like cell hyperplasia. Tumors are present at initial endoscopy in only 2.4% of patients, suggesting that hypergastrinemia alone is probably insufficient for tumor development. Further, chronic PPI use and vagotomy are not associated with gastric NETs, so there must be co-factors. Type I gastric NETs are benign. Overall survival rates are excellent; disease-specific survival approaches 100%. Metastases are rare. The metastatic potential is proportional

Figure 14.4

Type I gastric NET (carcinoid) arises in a patient with chronic atrophic gastritis. (**a**) Type 1 gastric carcinoid; (**b**) Type 1 gastric carcinoid (close-up)

to tumor size and infiltration, but there is no correlation between multicentricity and metastases. Outcome even in the presence of metastases is excellent (75% survival at 5 years). Despite a high frequency of type I gastric NETs, there is limited experience with metastases.

Type II gastric NETs account for 5–8% of gastric NETs. They are associated with MEN1 and ZES and have intermediate malignant potential (Fig. 14.5a, b). The synergy of the presence of the tumor-suppressor gene mutation on chromosome 11 and the hypergastrinemia of ZES associated with MEN1 promotes the development of gastric NETs in 23% of MEN1 patients. Type II gastric NETs are much more frequent in MEN1/ZES than in patients with sporadic ZES (without MEN1). Gastric NETs occur in less than 1% of patients with sporadic ZES. Type II gastric NETs are relatively indolent, but they do have a greater metastatic potential than type I tumors, which is approximately 10–30%. Further, type II tumors may de-differentiate to type III tumors, which have a worse prognosis. Whereas type I gastric NETs are limited to the body and fundus of the stomach, type II NETs occur diffusely in the stomach, including the gastric antrum.

Type III gastric NETs (about 15–20% of gastric NETs) arise sporadically and are the most aggressive subtype; between 50% and 100% metastasize (Fig. 14.6). Their development and biology is unrelated to gastrin concentration. They are often larger than 2 cm and are usually located in the antrum. They commonly produce 5-hydroxytryptophan (5-HT) rather than serotonin. Carcinoid syndrome is a rare complication of gastric NETs (<1%), which is usually associated with type III tumors having liver metastases.

Figure 14.4

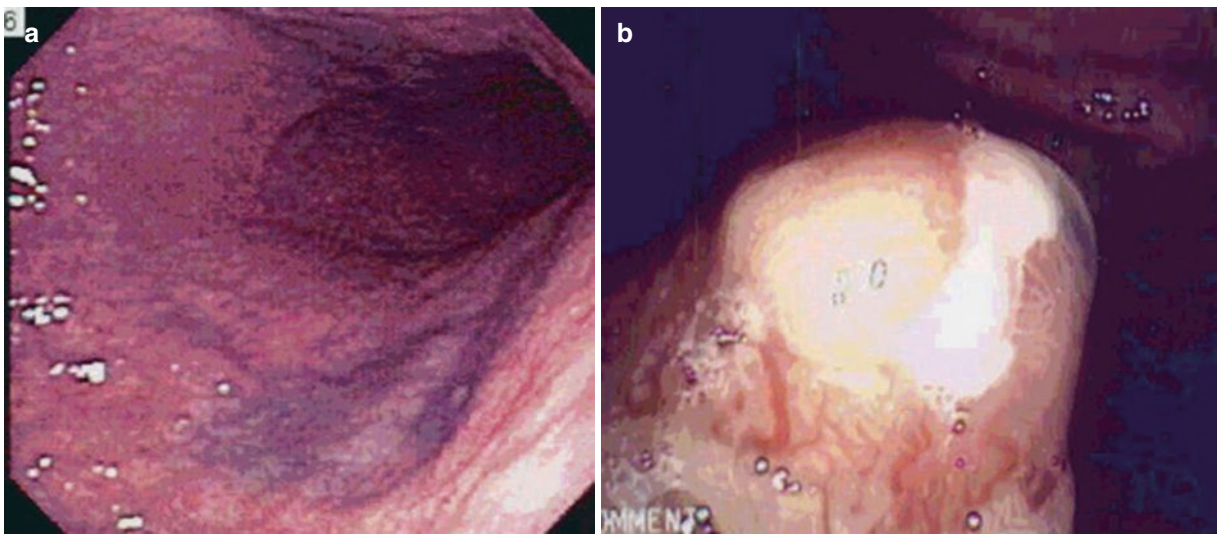


Figure 14.5

Type II gastric NETs (carcinoid). (**a**) Type 2 gastric carcinoid; (**b**) Type 2 gastric carcinoid (CT)

Figure 14.6

Type II gastric NETs (carcinoid)in setting of MEN1/ZES with de-differentiation of one tumor to Type III. This patient required total gastrectomy and had lymph node metastases

Figure 14.5

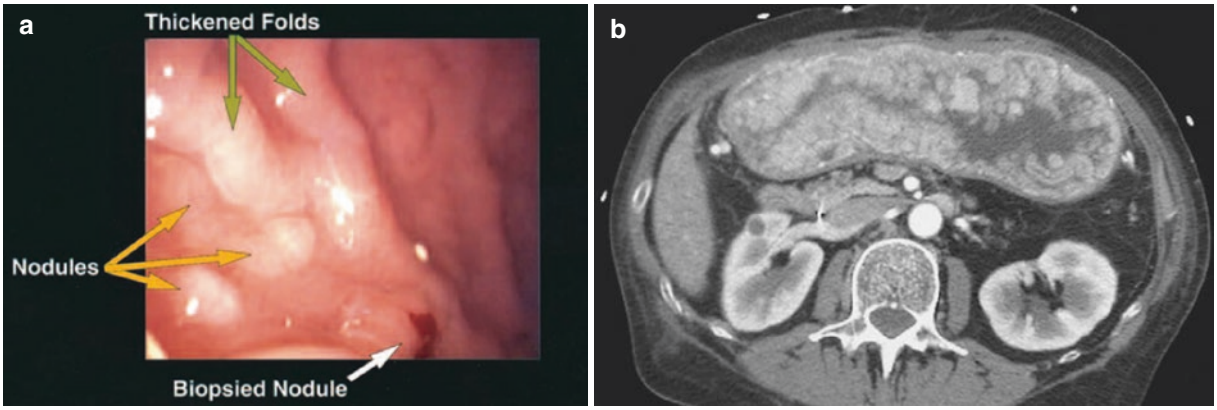
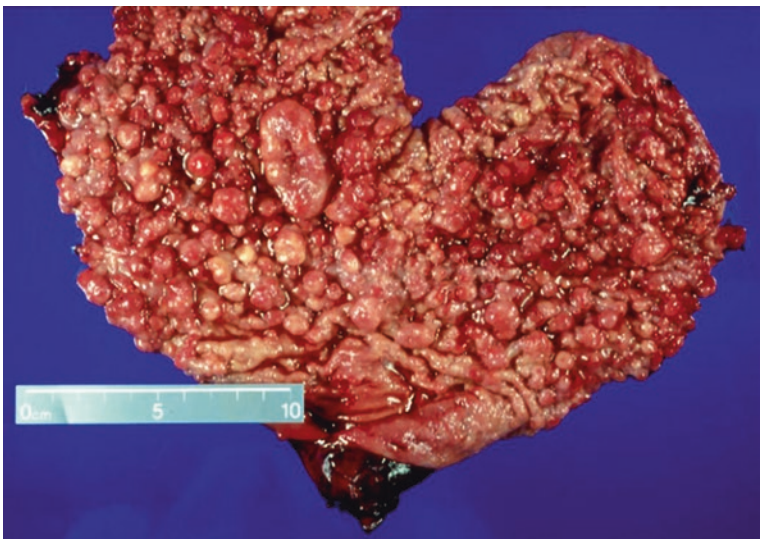


Figure 14.6



14.2.2 Treatment and Surgery

14.2.2.1 Surveillance and Local Resection

Management of gastric NETs is determined by subtype and whether the disease is localized or metastatic. As the commonest subtype (type I) is benign, simple surveillance or endoscopic excision is employed for small tumors. Surveillance is recommended for type I NETs smaller than 1 cm. For tumors between 1 and 2 cm that are confined to the mucosa and submucosa, endoscopic mucosal resection is recommended, but resection must be complete. Endoscopic resection can be easily repeated provided that tumors do not grow beyond 1 cm. The TNM staging system uses 1 cm in size as a cutoff to define T1/2 tumors, although there is inconsistency in guidelines as to whether tumors between 1 and 2 cm in size should be treated with local resection.

Surgery should be performed in cases of involvement beyond the submucosa or when there are positive margins after endoscopic resection or local excision (e.g., wedge resection). For type I gastric NETs, surgery is almost never required. Though antrectomy removes the source of gastrin hypersecretion and was previously recommended by some, most experts no longer recommend this technique. A simple wedge resection or localized excision followed by endo-

Figure 14.7

For type III gastric NETs (carcinoid), resect the stomach by subtotal or total gastrectomy plus D2 lymph node dissection. (**a**) Total gastrectomy. (**b**) EEA stapler to perform esophago-jejunostomy. (**c**) Closure of site where EEA entered jejunum with TA 60 stapler

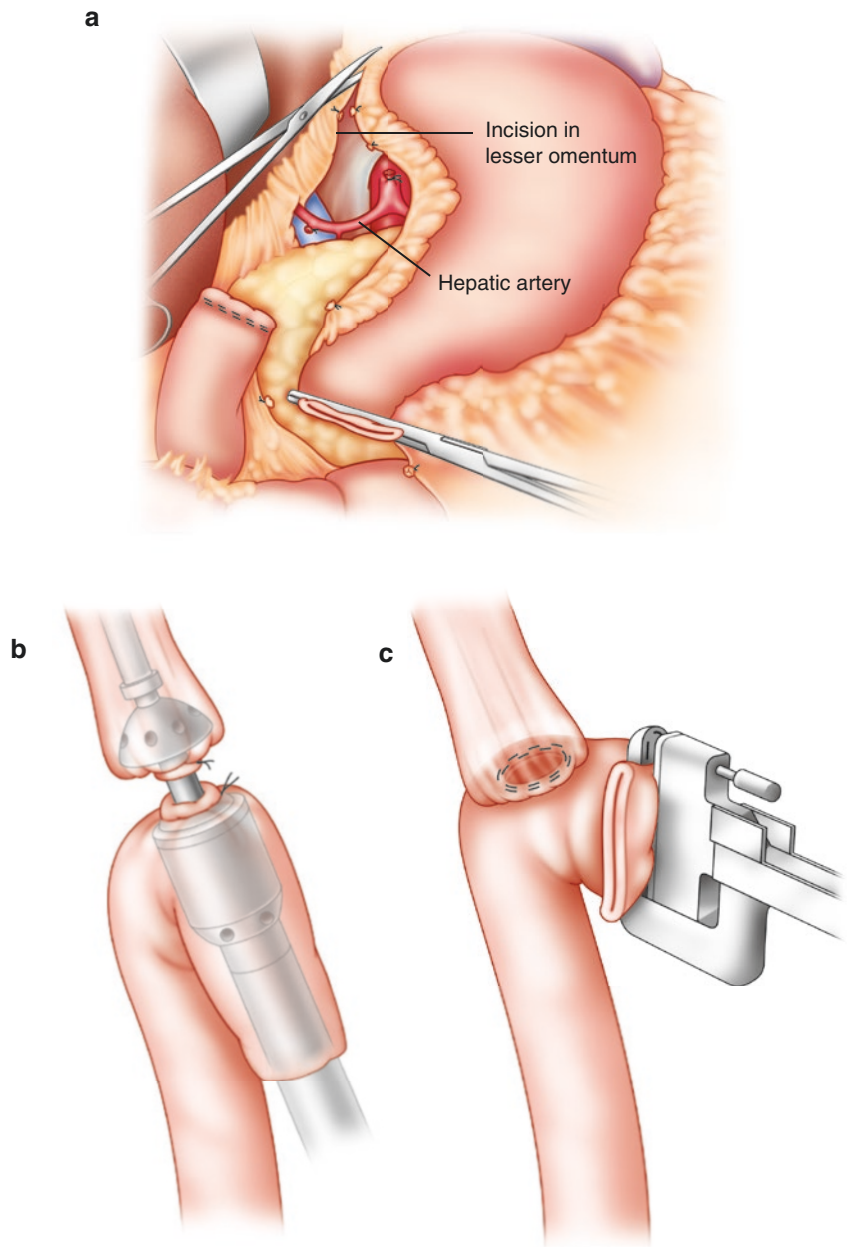
scopic surveillance is considered more appropriate. Follow-up for small type I NETs is yearly endoscopy, or endoscopy every 24 months if the case is stable and nonrecurring.

For type II tumors, subtotal or total gastrectomy may be necessary depending on the extent of disease and whether the tumor is larger than 2 cm; otherwise careful surveillance is indicated. For type III gastric NETs, subtotal or total gastrectomy plus D2 lymph node dissection is necessary to remove all tumors (Fig. 14.7a–c). Follow-up for more aggressive tumors is standard imaging plus or minus octreoscan.

14.2.2.2 Operative Technique for Subtotal or Total Gastrectomy with D2 Lymph Node Dissection

Exposure of the upper abdomen depends on the patient's build. For thin and normal-build patients, the upper abdomen is exposed through a midline incision from the xiphoid process of the sternum, extended just inferior to the umbilicus. For more rotund patients, a bilateral subcostal incision is made approximately 1–2 finger breadths inferior to the costal margin. After careful exploration of the abdomen to exclude distant metastases, the greater omentum is dissected off the transverse colon in an avascular plane from the

Figure 14.7



hepatic flexure to the splenic flexure. The omentum remains attached to the stomach and the lesser sac is exposed. The dissection then progresses proximally across the hilum of the spleen toward the hiatus. The correct plane is anterior to the pancreas, and thus the splenic vessels and pancreas are not affected. The short gastric vessels are divided with the LigaSure™ (Covidien, Mansfield, MA) up to the point of proximal transection, either the stomach in subtotal gastrectomy or the left crus of the diaphragm for total gastrectomy. Dissection is also performed distally toward the duodenum by dividing the right gastroepiploic artery, identifying the pyloric vein of Mayo, and exposing the duodenum away from the pancreas. Superiorly, the right gastric artery is divided to enhance exposure of the duodenum. The duodenum is secured with a blue load of the TA™ 60 stapler (Covidien). The TA™ 60 stapler is again used to place a second staple line on the divided duodenum to minimize spillage. Then the staple line on the duodenal stump is oversewn with a running, full-thickness 3-0 PDS suture. All the lymph nodes along the lesser curvature of the stomach are excised by opening the gastrohepatic ligament, skeletonizing the right gastric artery and the hepatic artery. The left gastric artery is divided at its origin with an Endo-GIA™ 30-mm stapler (Covidien) with a white or vascular load. This dissection should remove all the lymph nodes along the left gastric artery, common hepatic artery, celiac axis, splenic artery, and proper hepatic artery. For a subtotal gastrectomy, the stomach is divided 5 cm proximal to the tumor, using a TA™ 90 stapler with a green load. If a total gastrectomy is necessary, the right crus of the diaphragm is dissected to mobilize the esophagus for transection proximal to the stomach. It is important to remember to feel for the location of the nasogastric tube; if it is present at the point of transection, ask the anesthesiologist to pull it back so it will not be stapled into the margin. If the esophagus is being divided, placing a 3-0 silk seromuscular suture on the medial and lateral wall will prevent it from retracting after transection with a #10 blade. The pathologists should examine the specimen, which includes the stomach and the D2 lymph nodes, to determine the status of the proximal and distal margins. If tumor is present at the margin of transection, more tissue must be removed to attain a negative margin. Once there is no tumor at the margin, reconstruction can proceed.

The reconstruction is usually done by Roux-en-Y for either a subtotal or total gastrectomy. To obtain a Roux limb of jejunum, one measures approximately 20 cm distal to the ligament of Treitz, where the mesentery is most elongated. A GIA™ 55-mm stapler is used to divide the jejunum and the LigaSure™ is used to divide the mesentery. The distal segment of jejunum is brought through the mesentery of the transverse colon and anastomosed to either the esophagus or the remaining stomach. If the procedure is a subtotal gastrectomy, we anastomose the jejunum to the stomach in a side-to-side functional end-to-end manner with a GIA™ 55-mm stapler using a green or blue load. Where the stapler entered the stomach and jejunum, we close with a running 3-0 PDS suture and oversew it with a 3-0 silk seromuscular (Lembert) suture. Some surgeons staple across the area where the GIA™ entered the gut with a TA™ 60 stapler. We perform the jejunojejunostomy exactly the same way as the gastrojejunostomy except that we use a blue load with the GIA™ 55. If we do a total gastrectomy, we reconstruct with the EEA stapler (Fig. 14.7b). We place a running purse-string suture of full-thickness 2-0 Prolene on the esophagus. We use a 29-mm EEA stapler, place the anvil in the esophagus, and tie the purse-string. We then bring up the Roux limb that we plan to anastomose to the esophagus. We remove the staple line on the end of the limb, lubricate the shaft of the EEA stapler, insert it into the jejunum for a distance of 5–6 cm, and then pop out the post that attaches to the anvil through the antimesenteric side of the bowel. We then couple it to the anvil and anastomose the esophagus to the antimesenteric side of the jejunum with the EEA stapler. We remove the stapler from the bowel and pass the nasogastric tube slightly across the new anastomosis. We close the jejunum where the EEA entered the bowel with a blue load of the TA™ 60 (Fig. 14.7c). We examine the two staple rings (donuts) to be certain that they are intact. We place saline solution around the area of the anastomosis and a bowel clamp distal to it on the jejunum. We ask the anesthesiologist to insufflate with approximately 100 mL of air to distend the anastomosis, which is submerged in a pool of liquid. We then look for air bubbles that indicate a leak. If there are bubbles or there are not two intact donuts, we revise the anastomosis. Once we are certain that the EEA anastomosis is intact, we then close the abdomen. We do not routinely place drains or a feeding jejunostomy tube in these patients.

Suggested Reading

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4. Norton JA, Melcher ML, Gibril F, Jensen RT. Gastric carcinoid tumors in multiple endocrine neoplasia-1 patients with Zollinger-Ellison syndrome can be symptomatic, demonstrate aggressive growth, and require surgical treatment. Surgery. 2004;136:1267–74.
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Part V

Pancreas

Pancreaticoduodenectomy for Neuroendocrine Tumors

15

Albert Amini, Douglas B. Evans, and Kathleen K. Christians

15.1 Introduction

Pancreatic neuroendocrine tumors (PNETs) comprise a spectrum of slower-growing neoplasms (in comparison with adenocarcinoma of the pancreas) that arise from the pancreatic islets. Because patients with PNETs have a different natural history than those with adenocarcinoma, they present a different spectrum of management challenges. For example, unlike patients with pancreatic adenocarcinoma, patients with PNETs:

- May have survival durations measured in years, even with metastatic disease
- Often require complex management of the pancreatic tumor (local disease) because of their favorable survival outlook—especially in the setting of a large primary tumor, biliary obstruction, intravascular extension of tumor, or adjacent organ involvement
- May benefit from concomitant resection of both the primary tumor and metastases, which are most often in the liver
- May demonstrate dramatic responses to systemic therapy, with significant change in the size of the primary tumor or associated metastases.

The current practice at our institution (Medical College of Wisconsin, Milwaukee) is to stage the disease with high-quality multidetector (multi-slice) CT images of the pancreatic tumor. Similar to the criteria for adenocarcinoma, we use objective CT criteria to determine the resectability status of the primary tumor based upon the relationship of the pancreatic tumor to the superior mesenteric artery (SMA) and celiac axis. Encasement (>180° involvement of the vessel by tumor) of the celiac axis or the SMA, or occlusion of the superior mesenteric–portal venous (SMV/PV) confluence without technical option for venous reconstruction are considered criteria for a tumor's unresectability [1, 2]. The one exception to this general guideline includes celiac encasement that is amenable to celiac resection [3], with or without reconstruction of the common hepatic artery. Similar to our philosophy on local-regional management of pancreatic adenocarcinomas, we generally do not operate on patients in whom a complete gross resection of the primary tumor is not possible [4].

Accurate preoperative diagnosis and staging of the primary tumor is necessary to ensure the correct treatment. We have a liberal approach to the use of pretreatment endoscopic ultrasound fine needle aspiration (EUS-FNA) biopsy and routinely obtain a Ki-67 index and assessment for O^6-methylguanine DNA methyltransferase (MGMT) deficiency. As a general rule, tumors of high grade (grade 3), with a mitotic count of more than 20 per 10 high-powered fields, or a Ki-67 proliferation index of more than 20% represent highly aggressive malignancies that should be handled differently than well-differentiated (low to intermediate grade) PNETs [5]. These patients receive induction chemotherapy prior to surgical resection. There is also evidence that MGMT deficiency can predict treatment responses to temozolomide—information that is very important for patients with large primary tumors of borderline resectability or those with liver metastases for whom a combined resection of the primary tumor and the metastases is being considered [6].

We proceed with resection of localized, nonmetastatic disease confined to the pancreas if a gross complete resection can be performed. If radiographically occult liver metastases are found at the time of the operation, they are removed and/or ablated at the time of operation if possible. If the liver metastases are of small volume but diffuse (whether found prior to surgery or as an unexpected finding at the time of operation), the primary tumor is usually still removed because of the potential for major morbidity from it, and because of the relatively favorable anticipated survival of the patient. In the setting of known metastatic disease or a large,

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J.R. Howe (ed.), *Endocrine and Neuroendocrine Surgery*, Springer Surgery Atlas Series, DOI 10.1007/978-3-662-54067-1_15

borderline-resectable primary tumor, we often consider systemic therapy as a "bridge" to resection. As treatments for metastatic disease become more effective, the rationale for aggressive management of the primary tumor despite the presence of extrapancreatic disease may become even more compelling. However, in the setting of a high-risk, complicated operation directed at the primary tumor (with or without the need for concomitant liver resection or ablation), treatment sequencing will likely emphasize a surgery-last strategy (after induction systemic therapy) to identify those patients most likely to benefit from large, multiorgan resections. When dealing with a resectable primary tumor and resectable liver metastases, we usually remove the pancreatic tumor first. If that procedure goes well, we then consider liver resection/ablation under the same anesthesia induction, but we often use a two-stage procedure if the operation is of long duration or increased complexity [5].

Occasionally, an extended operation is required to achieve complete tumor resection of PNETs. Data from our institution has demonstrated the safety of segmental resection of the superior mesenteric vein (SMV) or SMV/portal vein(PV) confluence when necessary to allow complete tumor resection. When there is tumor encasement at the level of the splenic vein (SV) junction, SV transection may result in left-sided or sinistral portal hypertension if the inferior mesenteric vein (IMV) does not provide for retrograde SV decompression. In such cases, when the IMV does not enter the SV (and enters directly into the SMV), we have performed a distal splenorenal shunt (DSRS) at the time of SMV-PV resection and reconstruction (see Step 7 below). We have also used a DSRS combined with a mesocaval shunt (MCS; SMV sewn to the inferior vena cava with the use of an interposition graft) in the setting of cavernous transformation of the PV owing to significant narrowing or short segment occlusion of the PV or SMV/PV confluence (see Step 8) [7, 8]. These operations represent the highest level of technical complexity and are offered only to very carefully selected patients of suitable risk, often after a period of induction therapy. Arterial resection is occasionally performed but usually is limited to cases of isolated tumor involvement of the hepatic artery at the level of the gastroduodenal artery origin, or rarely, the celiac axis.

Management of patients with advanced PNETs (locally advanced pancreatic tumors and distant metastases) requires an understanding of the disease process (natural history and patterns of disease progression or recurrence) and emphasizes a multimodality therapeutic approach. Treatment options include cytotoxic chemotherapy to include tyrosine kinase inhibitors and inhibitors of the mTOR pathway, biologic therapy with somatostatin analogues and interferon, and ablative approaches such as hepatic artery embolization/chemoembolization (TACE) and radiofrequency or microwave ablation. As stated previously, systemic therapy is also being used as a bridge to other therapies including surgery; occasionally, systemic therapy may convert a patient with unresectable tumors into a patient that can be rendered disease-free by surgery. The complexity introduced by the ever-increasing options for local and distant treatment of patients with PNET now require that multidisciplinary input from physicians of many specialties be a consistent part of the care of all patients.

15.2 Surgical Technique

With regard to the technical aspects of pancreaticoduodenectomy (PD), the steps of this operation in a patient with PNET are similar to how the operation is performed in patients with the more common diagnosis of adenocarcinoma. The operation involves the en bloc removal of the pancreatic head, duodenum, gallbladder, and bile duct, along with the gastric antrum [9].

15.2.1 Step 1: Exposure of the Infrapancreatic Superior Mesenteric Vein (SMV)

We routinely use a midline upper abdominal incision and the Thompson retractor. When opening the abdomen, the falciform ligament is preserved to cover the gastroduodenal artery (GDA) stump prior to abdominal closure. The lesser sac is entered by mobilizing the greater omentum up and off of the transverse colon. The loose attachments of the posterior gastric wall to the anterior surface of the pancreas are then divided. The hepatic flexure of the colon is freed from its retroperitoneal attachments, exposing the pancreatic head and duodenum. The visceral peritoneum along the inferior border of the pancreas is then incised from the patient's left of the middle colic vessels to the patient's right and inferiorly to expose the junction of the middle colic vein and SMV; the anterior surface of the SMV is then exposed medial to the uncinate process (Fig. 15.1). In patients of increased BMI with mesenteric foreshortening, the middle colic vein is often divided to prevent traction injury and tearing of this vessel. The retroperitoneal attachments of the small bowel and right colon mesentery are taken down to a much greater extent in patients with uncinate tumors if there is extension of tumor into the root of the small bowel mesentery, as often occurs with large PNETs. When necessary, the small bowel mesentery can be mobilized by incising the visceral peritoneum all the way up to the ligament of Treitz (Cattell-Braasch maneuver).

15.2.2 Step 2: Extended Kocher Maneuver

The Kocher maneuver is begun at the third part of the duodenum by identifying the inferior vena cava. All tissue medial to the right gonadal vein and anterior to the inferior vena cava is elevated, along with the pancreatic head and duodenum as the

dissection progresses in a cephalad direction. This dissection is continued medially to the left lateral edge of the aorta, with exposure of the anterior surface of the left renal vein (Fig. 15.2). A complete Kocher maneuver is necessary for the subsequent dissection of the pancreatic head from the SMA (Step 6). Particularly important is the division of the leaf of peritoneum that extends from the retroperitoneum onto the root of the small bowel mesentery; incision of this portion of peritoneum is perhaps the most important part of the Kocher maneuver and allows one to appreciate the origin of the SMA.

15.2.3 Step 3: Dissection of the Porta Hepatis, Hepatic Artery Exposure, Cholecystectomy, and Bile Duct Transection

The portal dissection is commenced by exposing the common hepatic artery (CHA) proximal to the right gastric artery and the gastroduodenal artery (GDA); this exposure is facilitated by removing the nodal tissue anterior to this vessel. Proximal identification of the CHA is critically important to help prevent injury to a redundant hepatic artery. Both the right gastric artery and the GDA are then ligated and divided (Fig. 15.3). Division of the GDA allows mobilization of the hepatic (common-proper) artery off of the underlying portal vein (PV), which is widely exposed along its anterior surface. Cholecystectomy is then performed, and the common hepatic duct is transected at or above its junction with the cystic duct. Following transection of the bile duct, bile cultures are sent if the bile is contaminated from the presence of an indwelling endobiliary stent. A bulldog clamp is often placed on the transected hepatic duct to prevent contaminated bile from soiling the right upper quadrant until biliary reconstruction is completed. Note that the PV should always be exposed and the location of the right hepatic artery noted prior to dividing the common hepatic duct.

Though the PV should be identified, it is not extensively mobilized until Step 6, at which time the stomach and pancreas have been divided. Care must be taken to avoid injury to the superior pancreaticoduodenal vein draining the pancreatic head at the superolateral aspect of the PV, in order to prevent significant bleeding when adequate exposure and vascular control have not yet been achieved.

15.2.4 Step 4: Transection of the Gastric Antrum (or the Duodenum, if Pylorus Preservation Is Planned)

The terminal branches of the left gastric artery are ligated and divided along the lesser curvature of the stomach prior to gastric transection. The gastroepiploic artery along the greater curvature of the stomach is individually ligated and divided. The stomach is then transected with a linear gastrointestinal (GIA) stapler at the level of the third or fourth transverse vein on the lesser curvature and at the confluence of the gastroepiploic veins on the greater curvature to complete a standard antrectomy (Fig. 15.4). The omentum is then divided at the level of the greater curvature transection.

In patients with small tumors that do not invade the pyloric region or are not accompanied by metastatic adenopathy in the peripyloric region, preservation of the pylorus may be considered. It should not be performed in patients with bulky tumors of the pancreatic head, neoplasms involving the first or second portions of the duodenum, or lesions associated with grossly positive pyloric or peripyloric lymph nodes. When pylorus preservation is performed, we divide the gastroepiploic arcade and the duodenum at least 2 cm beyond the pylorus, if possible. At the time of reconstruction, we trim a few more millimeters off of the duodenum to create the duodenojejunostomy 1–2 cm from the pylorus, to ensure an adequate blood supply to the duodenum.

15.2.5 Step 5: Transection of the Jejunum

The loose attachments of the ligament of Treitz are taken down with care to avoid injury to the inferior mesenteric vein (IMV) situated immediately to the patient's left, running caudal to cranial. The jejunum is then transected with a linear GIA stapler approximately 8–10 cm distal to the ligament of Treitz (Fig. 15.5), and its mesentery is sequentially ligated and divided with an energy device such as the LigaSure™ (Covidien, Mansfield, MA). This dissection is continued proximally to involve the fourth and third portions of the duodenum. The duodenal mesentery is divided to approximately the level of the aorta, allowing the devascularized segment of duodenum and jejunum to be reflected beneath the mesenteric vessels into the right upper quadrant.

15.2.6 Step 6: Transection of the Pancreas and Completion of the Retroperitoneal Dissection

The most important and difficult part of the operation involves complete mobilization of the SMV/PV confluence and separation of the specimen from the right lateral border of the SMA (SMA margin). We usually place traction/hemostatic sutures on the superior and inferior borders of the neck of the pancreas. This is especially important along the inferior border of the pancreas, where a small artery will be found in most patients. The pancreas is divided at the level of the pancreatic neck anterior to the SMV/PV confluence. We usually use cautery to divide the pancreas and we are very careful to aspirate the pancreatic fluid when entering the

Figure. 15.1

Exposure of the infrapancreatic superior mesenteric vein (*SMV*). The lesser sac is opened widely by elevating the omentum off the transverse colon and reflecting it cephalad with the stomach. The hepatic flexure is then mobilized inferior and towards the patient's left to expose the head of the pancreas and SMV inferior to the pancreatic neck

Figure. 15.2

An extended Kocher maneuver. All tissue anterior to the IVC and leftwards of the right gonadal vein is elevated along with the duodenum and pancreatic head and dissection carried out to the left of the aorta, thereby exposing the left renal vein. IVC inferior vena cava, Ao aorta

Figure 15.1

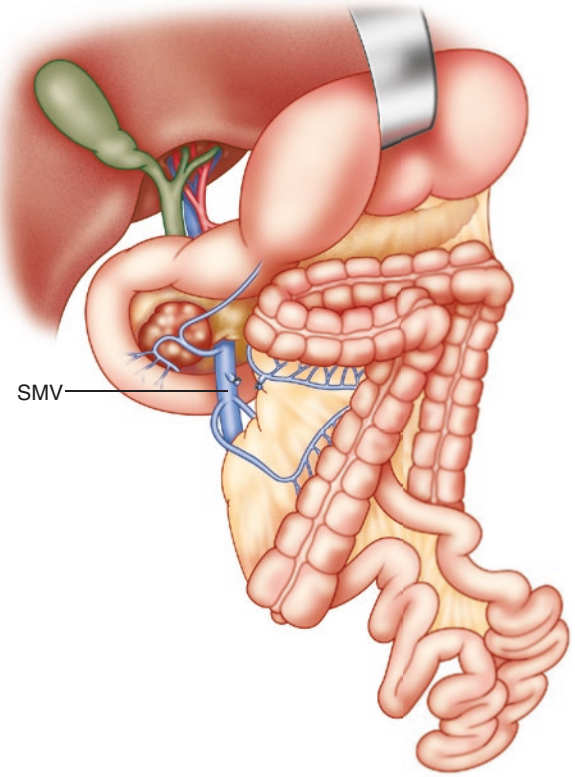


Figure 15.2

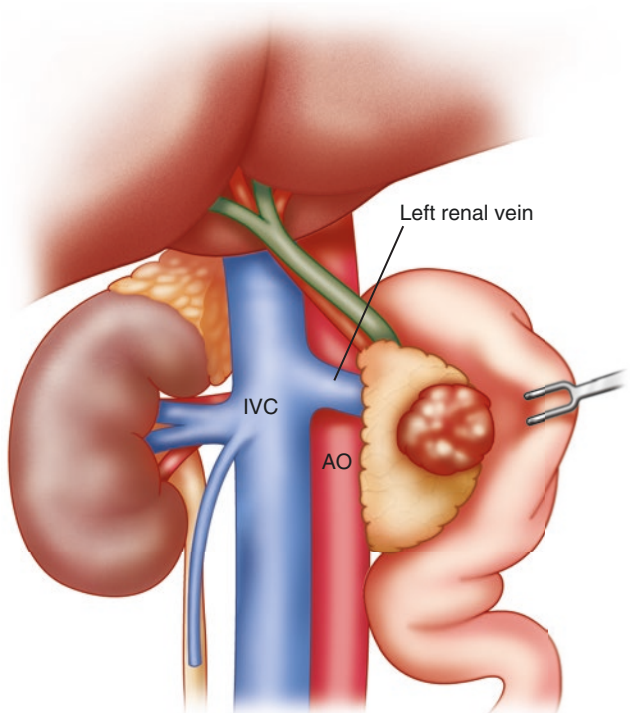


Figure. 15.3

Portal dissection, cholecystectomy, and bile duct transection. The common hepatic artery is identified proximally followed by the right gastric, gastroduodenal, proper and right and left hepatic arteries. The right gastric and gastroduodenal arteries are then ligated and divided. The gallbladder is removed. The common hepatic duct is then divided after first verifying the location of the portal vein and right hepatic artery

Figure. 15.4

Transection of the gastric antrum. The terminal branches of the left gastric artery are ligated and divided along the lesser curvature of the stomach, the gastroepiploic artery along the greater curvature of the stomach is individually ligated and divided, and the stomach is then transected with a linear gastrointestinal (GIA) stapler at the level of the third or fourth transverse vein on the lesser curvature and at the confluence of the gastroepiploic veins on the greater curvature, completing a standard antrectomy. CHA common hepatic artery, CHD common hepatic duct, SMA superior mesenteric artery, SMV superior mesenteric vein.

Figure 15.3

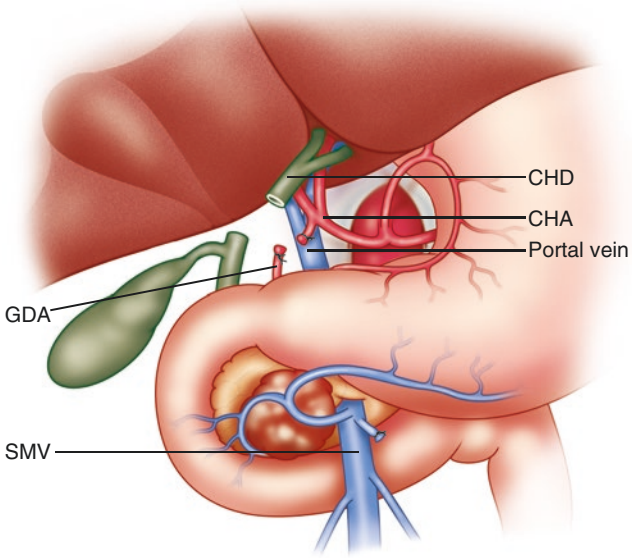
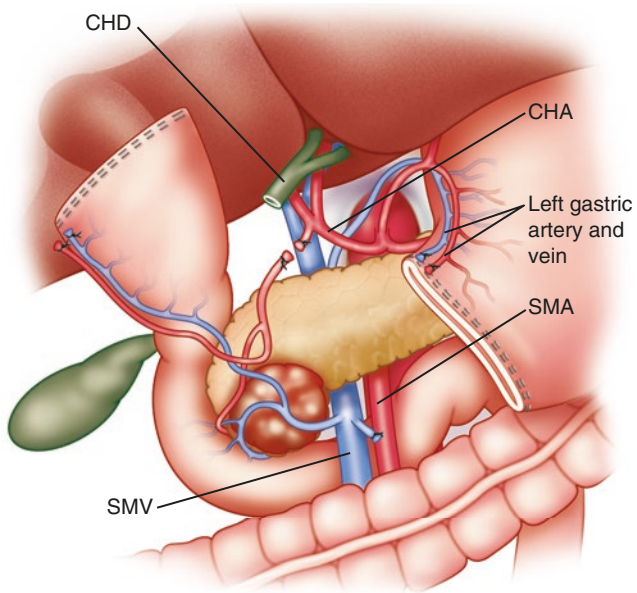


Figure 15.4



pancreatic duct. The pancreatic duct is most commonly posterior in location within the pancreas and lies just a few millimeters anterior to the SMV/PV. We prefer not to try to develop a plane of dissection anterior to the SMV/PV and posterior to the pancreatic neck prior to pancreatic transection, as bleeding prior to pancreatic transection can be difficult to control and complicates (unnecessarily) this part of the operation. If the tumor encases or is adherent to the SMV/PV, the pancreas is divided to the patient's left of the pancreatic neck in preparation for segmental venous resection. This is more difficult as the distal splenic vein is easily injured during pancreatic transection. Being very careful to locate the distal splenic vein before and during pancreatic transection (combined with experience) will minimize this complication.

The specimen is then separated from the PV and SMV by ligation and division of the small venous tributaries to the uncinate process and pancreatic head (Fig. 15.6a). Note that the relationship of the tumor to the lateral and posterior walls of the SMV/PV confluence can be directly inspected only after gastric and pancreatic transection. This relationship cannot be accurately assessed intraoperatively by simply developing a plane of dissection between the anterior surface of the SMV/PV confluence and the posterior aspect of the neck of the pancreas—which is why this age-old maneuver was abandoned.

Complete separation of the uncinate process from the SMV and its first jejunal branch is required to mobilize the SMV/PV confluence and reflect it to the patient's left. This is necessary for proper identification of the SMA unless the SMA has been exposed medial to the SMV (which we do in the setting of very large tumors and when the root of the small bowel mesentery must be resected with the pancreatic tumor). The first jejunal branch of the SMV originates from

Figure. 15.5

Transection of the jejunum. The attachments of the ligament of Treitz are taken down and the jejunum is then transected with a linear GIA stapler 8–10 cm distal to the ligament of Treitz. The mesentery is sequentially ligated and divided allowing the devascularized segment of duodenum and jejunum to be reflected beneath the mesenteric root into the right upper quadrant. SMA superior mesenteric artery, SMV superior mesenteric vein

the right posterolateral aspect of the SMV at the level of the uncinate process, usually travels posterior to the SMA, and enters the medial (proximal) aspect of the jejunal mesentery, giving off two or three branches directly to the uncinate process that need to be divided (Fig. 15.6b). If tumor involvement of the SMV at this location prevents dissection of the uncinate process from the SMV, the first jejunal branch can be divided. Injury to the SMV at the level of the first jejunal branch, or a tangential laceration in the first jejunal branch (as it courses posterior to the SMA), is hard to control and represents the most frequent cause of iatrogenic SMA injury (during efforts to control the venous hemorrhage). Whenever necessary (and certainly if the jejunal branch requires transection), we first expose the SMA medial to the SMV before dissecting the junction of the SMV and its first jejunal branch. Exposure of the SMA medial to the SMV is an underutilized technique that will always prevent an iatrogenic arterial injury or an unnecessary injury to the first-order branches of the SMV.

Medial retraction of the SMV/PV confluence allows identification of the SMA lateral to (to the patient's right of) the SMV/PV confluence and facilitates dissection of the pancreatic head and soft tissues off of the right lateral wall of the proximal SMA (Fig. 15.6c). Failure to fully mobilize the SMV/PV confluence and expose the SMA usually results in a positive margin owing to incomplete removal of the uncinate process and the mesenteric soft tissue adjacent to the SMA. Complete exposure of the SMV-PV and direct visualization of the SMA is especially important when dealing with large PNETs. A principle to remember is that the harder it is to expose the SMA, the more important it usually is.

Failure to identify and individually dissect and ligate inferior pancreaticoduodenal arteries (Fig. 15.6c) is the major cause of postoperative retroperitoneal hemorrhage, as these

Figure 15.5

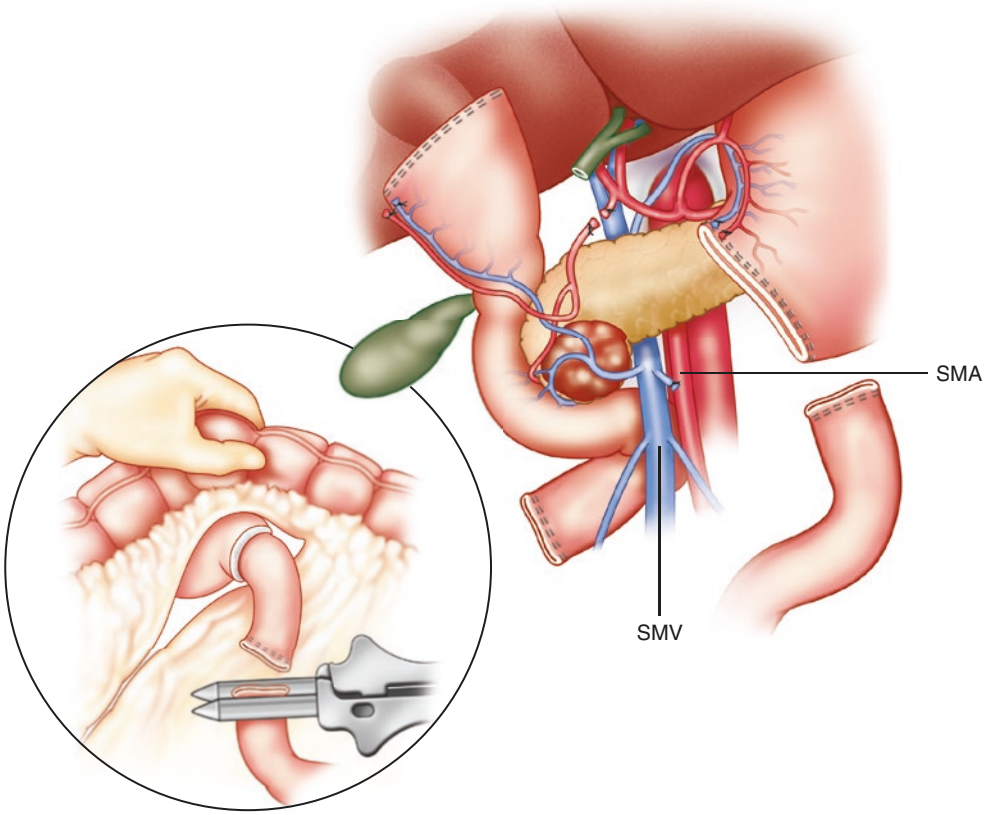
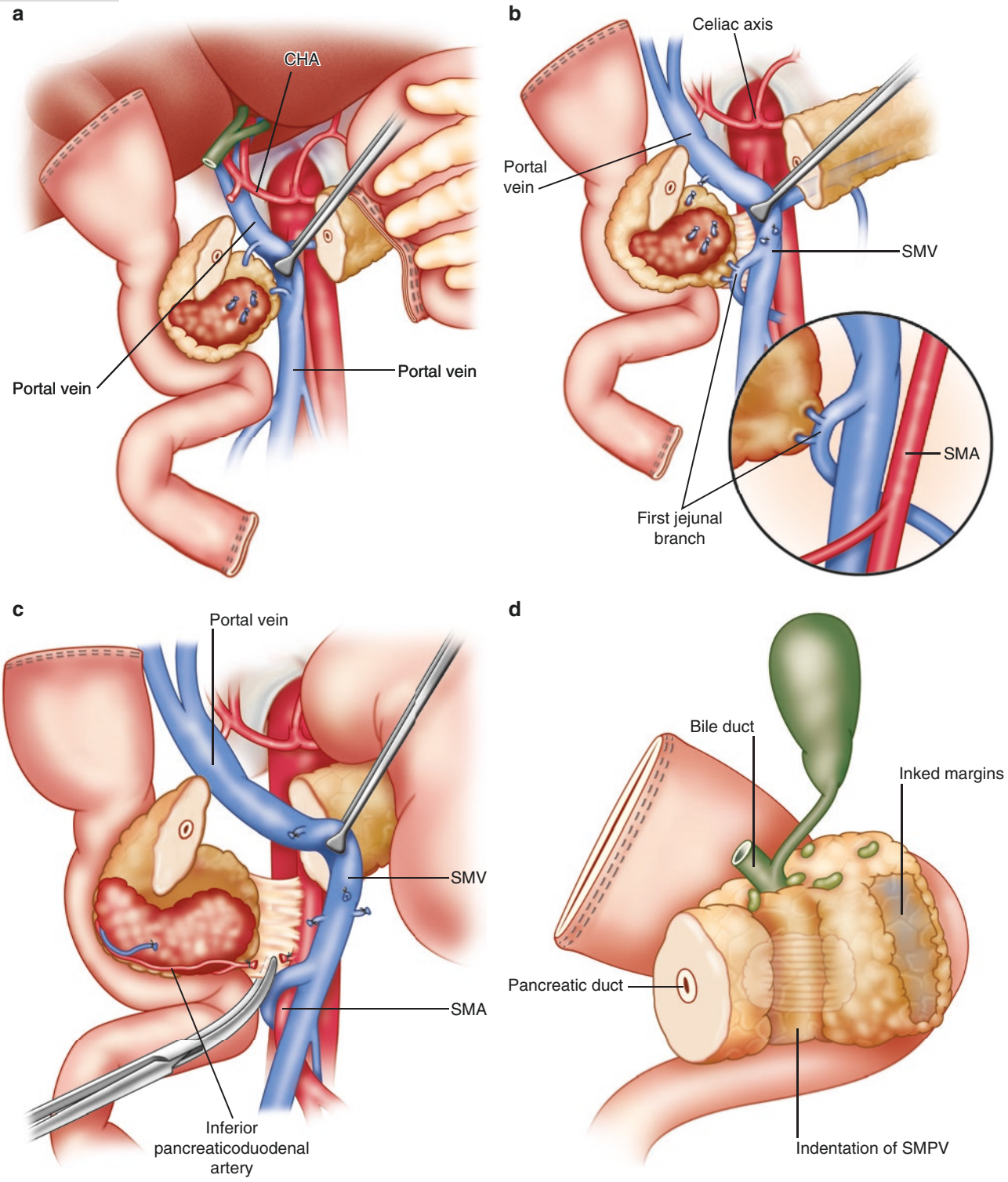


Figure. 15.6

Transection of the pancreas. (**a**) The specimen is separated from the portal vein (PV) and superior mesenteric vein (SMV) by ligation and division of the small venous tributaries to the uncinate process and pancreatic head. (**b**) Separation of the uncinate process from the SMV and its first jejunal branch. Inset illustrates small branches from the first jejunal branch entering the uncinate process. (**c**) Medial retraction of the superior mesenteric–portal venous (SMV/PV) confluence facilitates dissection of the pancreatic head and soft tissues off of the right lateral wall of the proximal superior mesenteric artery (*SMA*). The inferior pancreaticoduodenal arteries should be individually ligated and divided to prevent retraction and post pancreaticoduodenal hemorrhage. (**d**) The SMA margin (the soft tissue adjacent to the proximal 3–4 cm of the SMA) should be inked for pathologic assessment

Figure 15.6


a
CHA
Portal vein
Portal vein
b
Celiac axis
Portal vein
SMV
SMA
First jejunal branch
c
Portal vein
SMV
SMA
Inferior pancreaticoduodenal artery
d
Bile duct
Inked margins
Pancreatic duct
Indentation of SMPV

vessels may retract (if ligated with a large amount of mesenteric soft tissue) and bleed in the postoperative period.

The surgical specimen should be properly oriented to enable accurate assessment of the SMA margin (historically termed the retroperitoneal margin or uncinate margin) and other standard pathologic variables. The soft tissue adjacent to the proximal 3–4 cm of the SMA represents the SMA margin, which should be inked by the pathologist for permanent-section evaluation (Fig. 15.6d). This is especially important with adenocarcinoma and probably of lesser importance with a PD performed for PNET.

We perform frozen section analysis of the pancreatic and bile duct transection margins and re-resect them if a positive margin is found. Again, this is uncommon in patients with PNET, especially in the absence of multiple endocrine neoplasia type I, where multifocal disease is common.

15.2.7 Step 7: Vascular Resection and Reconstruction

Tumor adherence to the lateral wall of the SMV/PV confluence prevents dissection of the SMV and PV off the pancreatic head and uncinate process, thereby inhibiting medial retraction of the SMV/PV confluence (and lateral retraction of the specimen) (Fig. 15.7a). The standard technique for segmental venous resection involves transection of the splenic vein. Division of the splenic vein allows complete exposure of the SMA medial to the SMV and in most cases, provides increased SMV and PV length for a primary venous anastomosis, as they are no longer tethered by the splenic vein. The retroperitoneal dissection is completed by sharply dividing the tissues anterior to the aorta and to the right of the exposed SMA; the specimen is then attached only by the SMV/PV confluence. Venous resection is always performed with inflow occlusion (Rommel tourniquet) of the SMA to prevent small bowel edema (which makes pancreatic and biliary reconstruction more difficult). Systemic heparinization is employed prior to occluding the SMA. Vascular clamps are placed 2–3 cm proximal (on the PV) and distal (on the SMV) to the involved venous segment, and the vein is transected, allowing tumor removal (Fig. 15.7b). A generous 2- to 3-cm segment of SMV/PV confluence usually can be resected without the need for interposition grafting if the splenic vein is divided. The free ends of the vein are reapproximated using interrupted sutures of 6-0 polypropylene (Fig. 15.8). If the inferior mesenteric vein (IMV) enters the splenic vein, it will provide for splenic vein decompression

Figure. 15.7

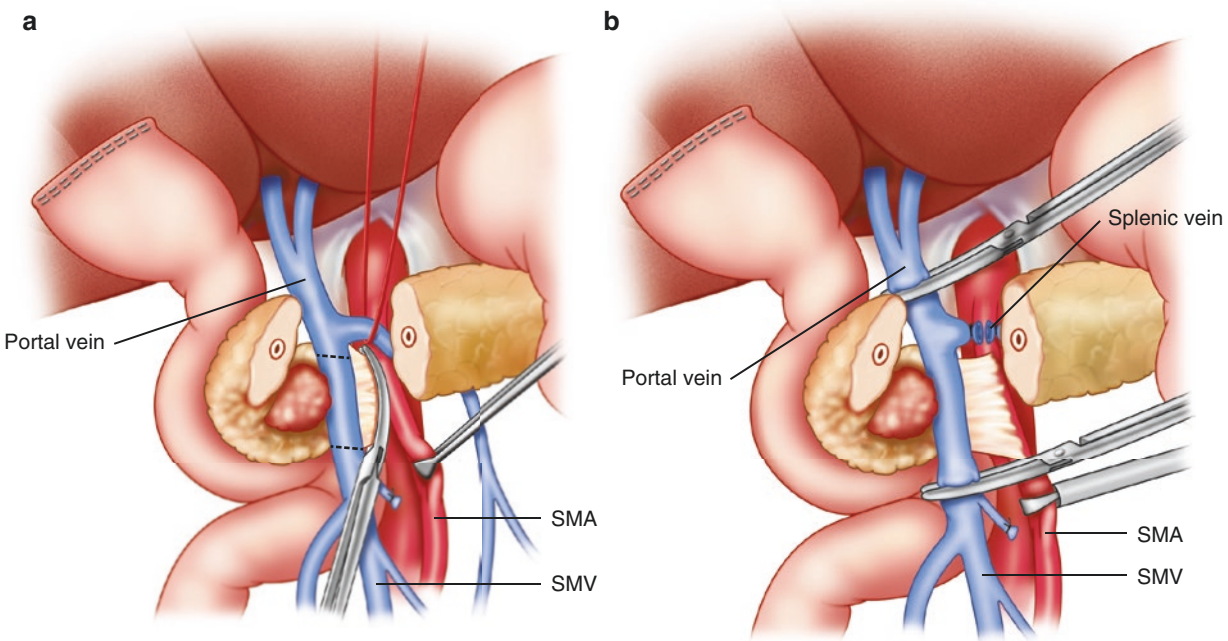
Vascular resection and reconstruction. (**a**) Tumor adherence to the lateral wall of the SMV/PV confluence prevents dissection of the SMV and PV off the pancreatic head and uncinate process, thereby inhibiting medial retraction of the SMV/PV confluence and lateral retraction of the specimen. (**b**) Segmental venous resection involves transection of the splenic vein which allows complete exposure of the SMA medial to the SMV and in most cases, provides increased SMV and PV length for a primary venous anastomosis. Vascular clamps are placed 2–3 cm proximal (on the PV) and distal (on the SMV) to the involved venous segment, and the vein is transected, allowing tumor removal

via retrograde flow to the systemic venous circulation. If the IMV enters the SMV and the splenic vein is divided, the patient is at risk for sinistral portal hypertension; in such cases we most commonly anastomose the distal splenic vein to the left renal vein in an end-to-side fashion to prevent the development of gastroesophageal varices.

15.2.8 Step 8: SMV Reconstruction When Tumor Involvement Is Limited to the SMV

When tumor involvement is limited to the SMV (inferior to the splenic vein confluence), we usually preserve the splenic vein–PV junction. Preservation of the splenic vein–SMV/PV confluence significantly limits the mobility of the PV and prevents primary anastomosis of the SMV (after segmental SMV resection), unless segmental resection is limited to less than 2 cm. Therefore, in most patients who require SMV resection with splenic vein preservation, an interposition graft (using the internal jugular vein) is necessary. Preservation of the splenic vein adds significant complexity to venous resection because it prevents direct access to the most proximal 3–4 cm of the SMA (medial to the SMV), as the splenic vein is anterior to the SMA. Venous resection and reconstruction is often performed after complete mesenteric dissection by separating the specimen first from the SMA. However, if the SMA dissection is expected to be difficult (due to tumor abutment of the artery) or if the PNET is very large, we would consider dividing the splenic vein to improve access to the root of mesentery. In such cases, the splenic vein would be anastomosed to the left renal vein unless the IMV provided adequate decompression, as discussed above. We have also used a temporary mesocaval shunt (MCS) to decompress the SMV and widely open the root of mesentery (leaving the splenic-SMV/PV junction intact); after tumor resection, the mesocaval shunt is converted to a PV anastomosis, thereby restoring flow in the SMV-PV. In the setting of cavernous transformation of the PV owing to significant narrowing or short-segment occlusion of the PV or SMV-PV confluence due to a large PNET (which may be accompanied by intraluminal tumor extension into the SMV-PV), we have used both a temporary mesocaval shunt and a distal splenorenal shunt to divert all portal flow during the time of tumor resection. In the setting of cavernous transformation of the PV, the portal dissection should not be attempted until all portal flow is diverted, because there is a risk of life-threatening hemorrhage if a

Figure 15.7



collateral vein in the porta hepatis is inadvertently entered. These techniques require significant experience with PD and vascular resection and reconstruction.

15.2.9 Step 9: Pancreatic Reconstruction

The pancreatic remnant is mobilized from the retroperitoneum and distal splenic vein for a distance of 2–3 cm to allow suture placement for the pancreaticojejunal anastomosis. We bring the transected jejunum retrocolic through a generous defect in the transverse mesocolon to the left of the middle colic vessels. We usually prefer a two-layer, end-to-side, duct-to-mucosal pancreaticojejunostomy. The outer row consists of interrupted 4-0 or 5-0 seromuscular monofilament sutures. The inner row consists of 5-0 interrupted monofilament sutures approximating full-thickness pancreatic duct to full-thickness jejunum. Posterior knots are usually tied on the inside, while the lateral and anterior knots are tied on the outside (Fig. 15.9). If a stent is used, it is placed across the anastomosis prior to securing the anterior sutures, so that it extends into the pancreatic duct and small bowel for a distance of about 2 cm each way.

15.2.10 Step 10: Biliary Reconstruction

Distal to the pancreaticojejunostomy, we create a one-layer, end-to-side hepaticojejunostomy with 4-0 or 5-0 absorbable monofilament sutures (Fig. 15.10). This anastomosis is not stented even when the common hepatic duct is of normal size. It is very important to avoid tension and leave adequate length between the pancreatic and biliary anastomoses; inadequate length between the anastomoses is the most common mistake in creating the pancreatic and biliary reconstruction.

Figure. 15.8

Vascular resection. Venous resection is always performed with inflow occlusion (Rommel tourniquet) of the SMA to prevent small bowel edema. Systemic heparinization is employed prior to occluding the SMA. The ends of the SMV and PV are anastomosed end-to-end using interrupted polypropylene sutures

15.2.11 Step 11: Gastric or Duodenal Reconstruction

The gastrojejunostomy is usually placed antecolic and is hand-sewn in two layers. A posterior row of 3-0 silk sutures is followed by a full-thickness inner layer of running absorbable monofilament sutures; an anterior row of silk sutures completes the anastomosis (Fig. 15.11a). We allow at least 45–50 cm between the hepaticojejunostomy and the gastrojejunostomy to prevent cholangitis from reflux of gastric contents. When the pylorus is preserved, the duodenojejunostomy is created in an antecolic, end-to-side fashion with a single-layer, hand-sewn technique using monofilament absorbable sutures (Fig. 15.11b). Again, the distance between the biliary and duodenal anastomoses should be approximately 45–50 cm, and we gently dilate the pylorus before completing the anastomosis. In most patients, a 10-Fr jejunostomy tube for postoperative enteral feeding is placed distal to the gastrojejunostomy using the Witzel technique. The falciform ligament is prepared as a pedicle flap and placed between the CHA and the afferent jejunal limb to cover the stump of the GDA. This strategy may help to prevent pseudoaneurysm formation at the GDA stump in the event of a pancreatic anastomotic leak, which would result in an abscess. Prior to abdominal closure, the abdomen is carefully irrigated with water and the small bowel is run to ensure proper alignment. The use of drains remains controversial: Many surgeons still drain the pancreaticojejunostomy, but we usually do not. In patients who require a large retroperitoneal or mesenteric dissection with disruption of lymphatics, we use an abdominal drain to manage ascitic fluid, which is usually self-limited but can be significant in the first few days after operation.

Figure 15.8

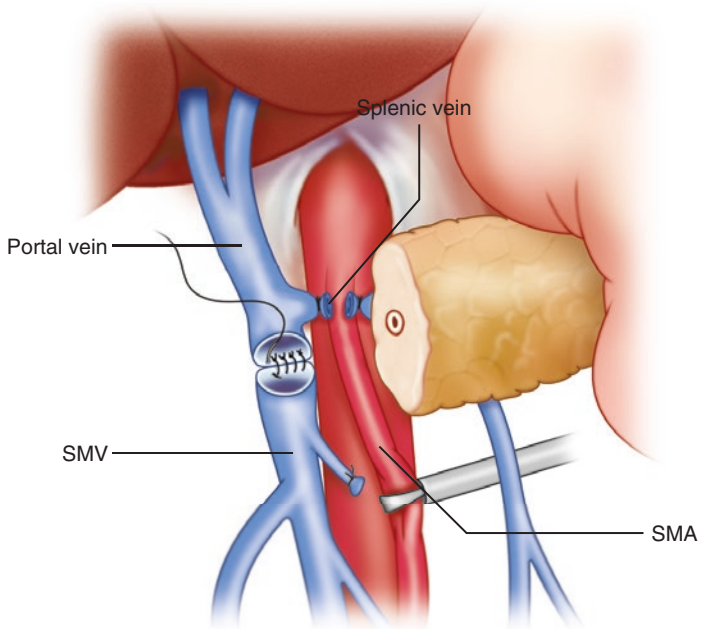


Figure. 15.9

Pancreatic reconstruction: pancreaticojejunal anastomosis. A two-layer, end-to-side, duct-to-mucosal pancreaticojejunostomy is created. The outer row consists of interrupted 4-0 or 5-0 seromuscular monofilament sutures. The inner row consists of 5-0 interrupted monofilament sutures approximating full-thickness pancreatic duct to full-thickness jejunum. Posterior knots are usually tied on the inside, while the lateral and anterior knots are tied on the outside

Figure. 15.10

Biliary reconstruction: hepaticojejunostomy. Distal to the pancreaticojejunostomy, a one-layer, end-to-side hepaticojejunostomy with 4-0 or 5-0 absorbable monofilament sutures is created

Figure 15.9

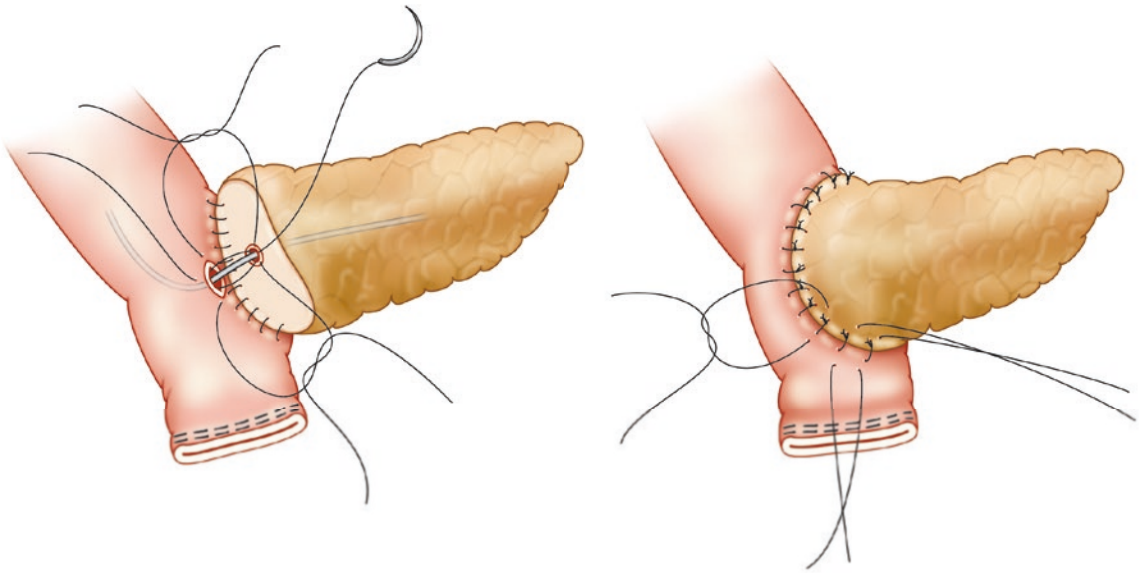


Figure 15.10

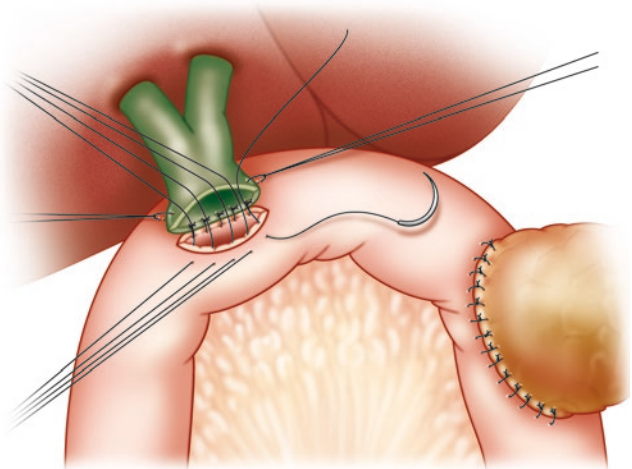
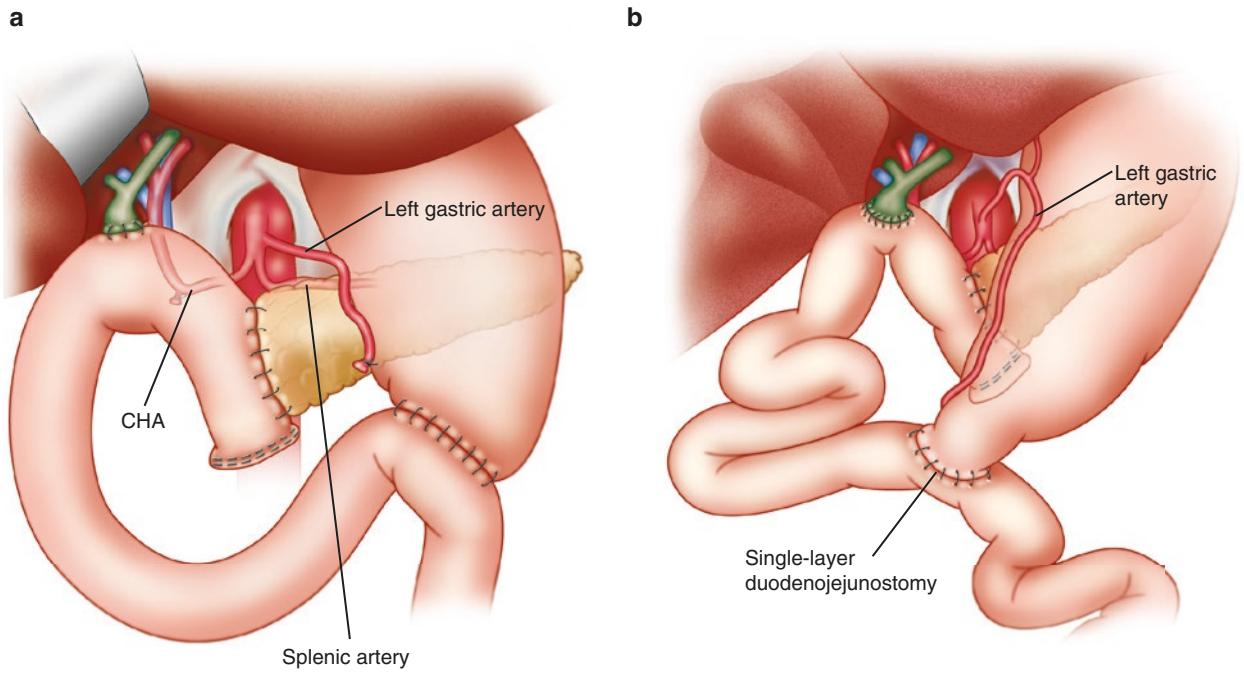


Figure. 15.11

(**a**) Gastrojejunostomy. The gastrojejunostomy is usually created 45–50 cm distal to the hepaticojejunostomy as an antecolic, hand-sewn, two layer anastomosis. A posterior row of 3-0 silk sutures is followed by a full-thickness inner layer of running absorbable monofilament sutures; an anterior row of silk sutures completes the anastomosis. (**b**) Duodenojejunostomy. When the pylorus is preserved, the duodenojejunostomy is created in an antecolic, end-to-side fashion with a single-layer, hand-sewn technique using monofilament absorbable sutures. The pylorus is dilated prior to completing the anastomosis. CHA common hepatic artery

Figure 15.11


a
Left gastric artery
CHA
Splenic artery
b
Left gastric artery
Single-layer duodenojejunostomy

15.3 Results and Conclusions

PD as described here is performed as a series of defined maneuvers, in an effort to reduce a complex operation into its less complicated component parts. Careful preoperative assessment of the patient and his or her local tumor-vessel anatomy using high-quality imaging is important to achieve the expected good outcome. PD performed at high-volume centers can be accomplished with 30-day/in-hospital mortality rates less than 2%. This should be the expected outcome for patients with PNET, as in the absence of a treatment-related complication, their life expectancy will usually be measured in years even with observation alone. Indeed, perioperative mortality is hard to justify. Attention to the details of operative technique to include individual venous and arterial anomalies will minimize blood loss and operative time. A standardized approach to postoperative care (pathways) will maximize the opportunity for a rapid recovery and avoid a lengthy hospital stay.

The goals of PD are to maximize local disease control and to increase the quality and length of patient survival (hoping for cure in patients with localized, potentially resectable primary tumors). For patients with PNETs, the decision to proceed with extended resection is perhaps the most difficult because survival for such patients without operative intervention is commonly measured in years. In the absence of extrapancreatic metastatic disease, the appropriate management of patients with locally advanced, surgically unresectable PNETs was previously a difficult therapeutic dilemma. In the era of more effective systemic therapies, however, systemic therapy has become the accepted standard in the hopes of experiencing significant tumor down-staging as a bridge to eventual surgical resection. The current and future treatments for patients with PNETs involve multimodality therapies, which will place an even greater emphasis on safe surgery.

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Open Distal Pancreatectomy

16

Charles M. Vollmer Jr and Jeffrey A. Drebin

16.1 Introduction

Historically, references to distal pancreatectomy (DP) date back to the late 1800s. Billroth is said to have performed resections of both the head and tail of the pancreas in 1884, but Trendelenburg supposedly preceded this feat by 2 years when he performed a DP with splenectomy for a sarcoma. However, the patient did not survive past the first postoperative day [1]. Still, DP was not performed with regularity for nearly a century thereafter. Among the many reasons were the paucity of obvious presenting symptoms for conditions of the distal pancreas, the inaccuracy of staging malignancies, difficulty in exposing the retroperitoneum, and excessively high morbidity and mortality rates. Interestingly, neuroendocrine diseases presented early opportunities for advancement, and Finney and Mayo published some of the first successful case reports [2, 3].

Today, indications for DP have expanded to include overt malignancies (adenocarcinomas of the pancreas and stomach, tumors metastatic to the pancreas), lesions with malignant potential (cystic neoplasms, neuroendocrine tumors, solid pseudopapillary tumor), and benign conditions (primarily pancreatitis and trauma). Nevertheless, DP is still performed infrequently: In a specialized pancreatic surgical practice, proximal resections will be two to three times more common than DP, and that ratio increases to 10:1 when pancreatic adenocarcinoma is the indication. This ratio reflects the relative rarity of discovering pancreatic cancer while it is still locally confined to the distal pancreas. Though distal resections for malignancies are relatively rare, in the contemporary era of radiographically identified "incidentalomas," premalignant cystic neoplasms and neuroendocrine tumors are being recognized with alarming frequency [4]. Many of these lesions are managed by surveillance, but DP is required for those with threatening features, and these are now the most common indications for DP. Meanwhile, segmental resection procedures for pancreatitis, which was the primary indication for DP 30 or 40 years ago, are waning over time as drainage procedures have become more popular.

Whereas reasonable indications for DP are now well established, controversies still surround technical considerations of the procedure. Foremost is the choice between minimally invasive surgery versus open exposure. Minimally invasive options for DP (addressed elsewhere in this Atlas) have proven to be safe but so far have shown only equivalence, not superiority, to open resection. Available evidence (generally from nonrandomized, highly selected case series) suggests that minimally invasive surgery offers improvements in wound complications, blood loss, spleen preservation, and duration of hospital stay, but not for metrics such as overall or major complications, pancreatic fistula, mortality, or oncologic survival [5]. Minimally invasive approaches are featured by select specialty institutions, but open resection remains the gold standard and is especially relevant in patients with previous abdominal surgery, obesity, pancreatitis, and malignancies, particularly when en bloc resection of adjacent organs may be required.

In terms of technique, most texts and surgical training programs traditionally have featured a classic retrograde (lateral-to-medial) dissection in which the spleen is first mobilized and then used as a handle to "lift" the distal pancreas from the retroperitoneum. This approach, commonly applied in the trauma setting, is associated with unnecessary blood loss. More importantly, standard oncologic principles are frequently compromised by bluntly dividing posterior tissue planes without directly visualizing and

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J.R. Howe (ed.), *Endocrine and Neuroendocrine Surgery*, Springer Surgery Atlas Series, DOI 10.1007/978-3-662-54067-1_16

optimizing resection margins or ensuring an adequate regional lymphadenectomy. Instead of this approach, this chapter describes an alternative, medial-to-lateral dissection philosophy in which vascular control is ensured before removal of the distal gland and the spleen. Essentially, this description represents the maneuvers that serve as a foundation for the RAMPS (Radical Antegrade Modular Pancreato-Splenectomy) procedure proposed by Strasberg et al. for resection of pancreatic cancers in the body and tail of the pancreas [6]. This approach not only reduces blood loss but also, more importantly, ensures better visualization and management of dissection planes that are important when there is malignant or inflammatory pathology.

16.2 Procedure

16.2.1 Step 1: Incision

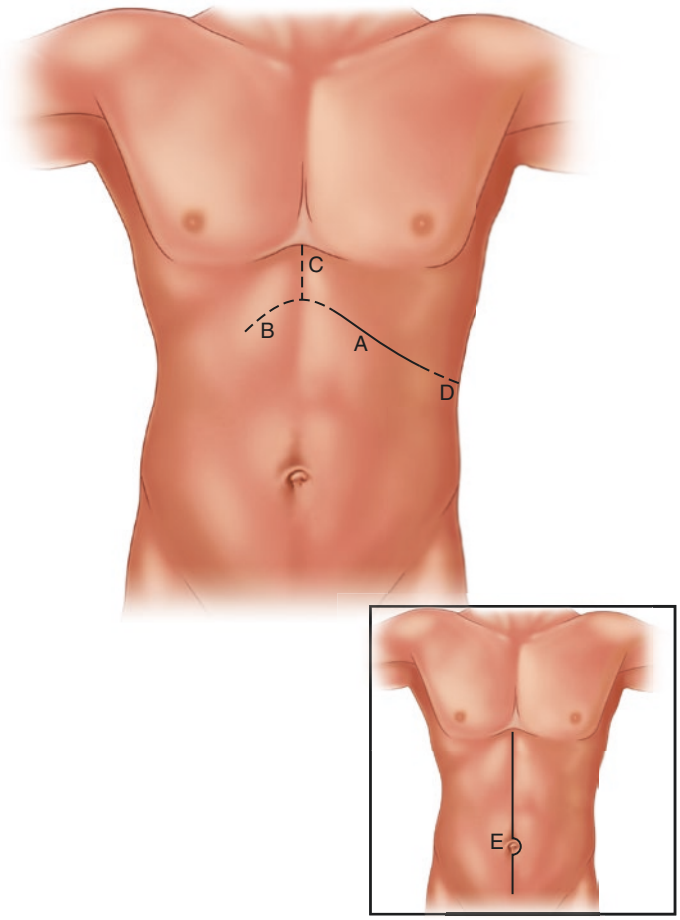
The retroperitoneal nature of the pancreas, coupled with its relationships with major vascular structures, mandates that exposure should not be compromised. For open DP on most patients, a left subcostal incision is the preferred approach—the one that offers the most flexibility. After administration of appropriate antibiotics (first-generation cephalosporin) and thromboembolism prophylaxis, this incision should be created about two fingerbreadths inferior and parallel to the costal margin (Fig. 16.1A). Depending upon variations of body habitus or the logistics of the procedure, certain exten-

Figure 16.1

Incision options for open distal pancreatectomy. (***A***) Left subcostal incision. (***B***) Subcostal extension across the midline. (***C***) Upward midline extension ("hockey stick"). (***D***) Lateral extension. (***E***) (*inset*), Standard upper-midline incision

sions from this baseline are available. If central dissection over the portal vein canal is anticipated, a soft-angled subcostal extension for a few centimeters across the midline to the right is useful (Fig. 16.1B). If celiac, supraceliac, hepatic, or high gastric dissection is required, an upward extension along the midline is sometimes useful (Fig. 16.1C). This is otherwise known as a hockey stick incision—the mirror image of the incision used for major hepatic resections on the right side. Lateral extension (Fig. 16.1D) is sometimes necessary for the particularly deep abdomen in the anterior-posterior plane, or for a barrel chest. The drapes should always be prepared lower towards the table on the left side in anticipation of this need. Finally, slight, aesthetic torsos with long, narrow-angled costal margins are generally amenable to a standard upper-midline incision (Fig. 16.1E). Finally, the umbilical ligament can ultimately be used as an autologous patch for the pancreatic transection line [7]. Foresight in preserving this option should occur at the outset of the operation. The upper abdominal, preperitoneal fat pad can be dissociated in continuity with the umbilical ligament and left attached to its origin from the umbilical fissure of the liver until later in the procedure.

Figure 16.1



16.2.2 Step 2: Isolation of the Splenic Artery and Identification of the Portal Vein

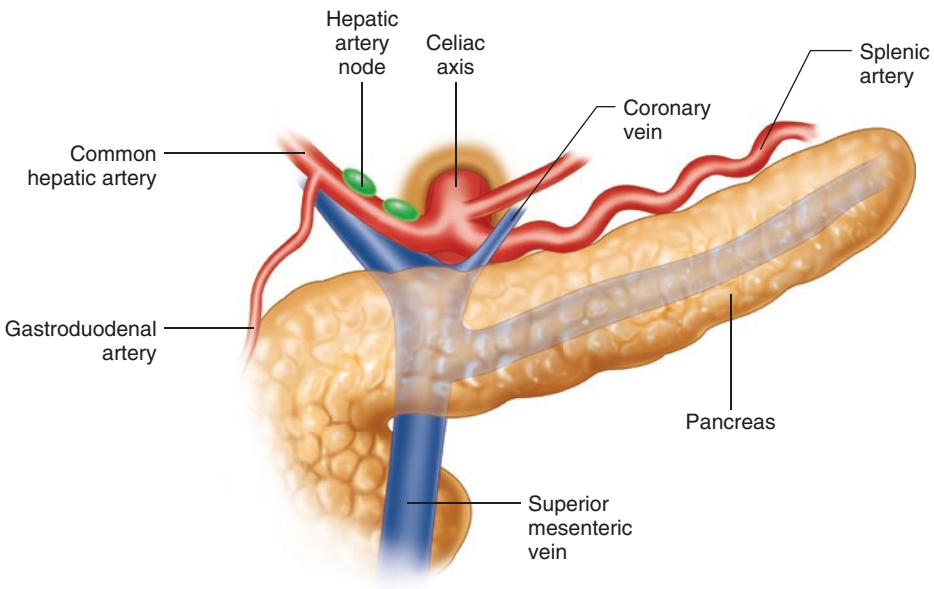
Performing an efficient and safe distal pancreatectomy with limited blood loss depends on early vascular control. First, the left lateral segment of the liver should be retracted superiorly against the diaphragm, using a self-contained retraction system. The central vasculature involved in this operation is initially accessed by dividing the membranous gastrohepatic ligament. Often this ligament is lacy in consistency and is transparent, so that the body of the pancreas is easily recognized through it. Sometimes the duodenohepatic ligament must be divided laterally, somewhat towards the bile duct. Then, inferior traction on the lesser curvature of the stomach will expose the zone of the celiac axis in a deeper plane (Fig. 16.2). A prominent, discoid lymph node (also known as the hepatic artery node or "Node of Importance") is commonly encountered first. This node can be lifted off the upper border of the neck of the pancreas relatively easily, which exposes the proper hepatic artery and often the takeoff of the gastroduodenal artery (GDA). Unlike in the Whipple procedure, it is not necessary to transect the GDA, which serves as a landmark for the right lateral-most border afforded for pancreatic transection in a DP. Between the proper hepatic artery and the pancreatic neck tissue lies a fairly thin layer of fibrofatty and lymphatic tissue shielding exposure to the anterior surface of the portal vein. Careful transection with cautery exposes the vein beneath and allows for development of the superior aspect of the portal vein "canal," which defines the neck of the pancreas.

Figure 16.2

Isolation of the splenic artery. After securing the landmarks shown in this figure, dissection laterally to the left along the upper border of the pancreatic body will identify the course of the splenic artery

Once these landmarks are secured, dissection can proceed laterally to the left along the upper border of the pancreatic body for a few centimeters. Here, the course of the splenic artery is identified, usually after first dissecting through some fibrofatty tissue. Within a few centimeters of its origin from the celiac axis, the splenic artery usually disappears within the tissue of the pancreatic body. It should also be recognized that its trajectory is more often posterior-to-anterior, arising deep from the retroperitoneum, rather than in a coronal left-to-right plane, as depicted in many texts. Length should be achieved along the splenic artery in preparation for its ultimate transection. A vessel loop or 2-0 silk suture can be loosely placed around it to ensure that inflow control to the pancreas and spleen can be swiftly accomplished should there be inadvertent bleeding later in the procedure. Two tips: First, the left gastric vein (also known as the coronary vein) courses to its insertion into either the portal vein or splenic vein in this zone. Generally, this vein runs posterior (deep) to the splenic artery, but not infrequently it may lie anterior to the artery (as depicted in Fig. 16.2). If so, it will require ligation to access the splenic artery, unless a generous amount of artery is available for ligation lateral to it. Second, dissection of this area may be impractical (if not impossible) exclusively from this window above the stomach, particularly in the obese. If so, better exposure is often achieved by dividing the gastrocolic omentum, as described in the next step. The body of the stomach can then be retracted superiorly to fully expose this region, and manual traction inferiorly upon the pancreatic neck and body "flattens" the dissection plane for better exposure.

Figure 16.2



16.2.3 Step 3: Exposure of the Lesser Sac and Division of the Short Gastric Vascular Arcade

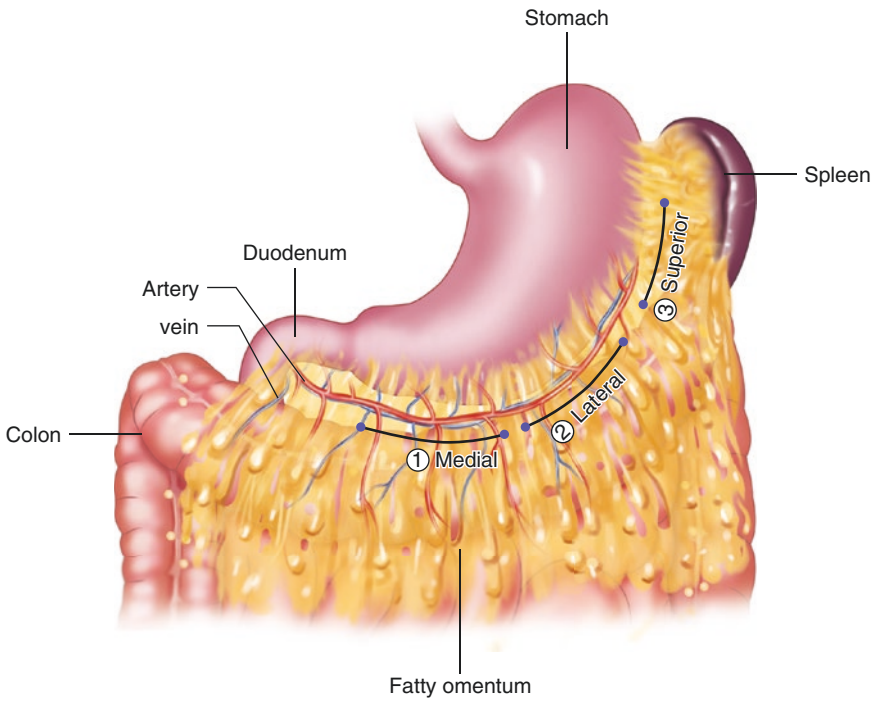
Once inflow control is obtained, full exposure of the pancreatic body and tail can be achieved by dividing the gastrocolic ligament (Fig. 16.3). The easiest area to start is just lateral to the line of the gastric incisura, where there is usually a transparent opening in the adipose tissue beneath the course of the gastroepiploic vascular arcade. Once the free space of the lesser sac is accessed, the omentum can be transected roughly halfway between the vascular arcade and the transverse colon inferiorly. Energy devices such as the LigaSure or Harmonic scalpel are efficient and hemostatic in this layer of thick adipose tissue. Dissection should proceed medially in such a way that the gastroepiploic vascular arcade is followed back

Figure 16.3

Exposure of the lesser sac and division of the short gastric vascular arcade. During lateral dissection along the greater curvature of the stomach, individual short gastric vessels are encountered coursing from the stomach to the splenic hilum. If splenectomy is planned, dissection and control of the lienogastric ligament should proceed superiorly to the upper pole of the spleen

to identify its insertion to the superior mesenteric vein (SMV). Then, lateral dissection will proceed superiorly along the greater curvature of the stomach; the individual short gastric vessels are encountered coursing from the stomach to the splenic hilum. If a Warshaw-type, spleen-preserving approach is chosen [8], this step should be withheld, so the spleen can remain vascularized through these vessels. If a traditional DP with splenectomy is performed, meticulous dissection and control of this lienogastric ligament should proceed superiorly to the upper pole of the spleen. Again, while these vessels can be individually ligated with sutures, mechanical coagulation devices, or even vascular staplers, have proven to be highly efficient. Care must be taken, however, to avoid thermal damage to the gastric wall. Next, superior retraction of the stomach against the liver and diaphragm allows for full exposure of the distal pancreas and the pathology of interest.

Figure 16.3



16.2.4 Step 4: Dropping the Splenic Flexure of the Colon

Exposure of the inferior border of the body and tail of the pancreas, and usually the pathology, requires complete mobilization of the splenic flexure of the colon, which can have variable placement in the left upper quadrant. Particular care should be taken in this dissection to prevent a traction injury, which will tear the splenic capsule and lead to annoying, if not dangerous, bleeding. Fig. 16.4 demonstrates a dissection along two fronts to achieve this objective. First, using electrocautery, the interface of the lateral aspect of the colon should be released along the "white line of Toldt" for a limited distance to allow for medial mobilization. The lower pole of the spleen will be encountered if this dissection is followed superiorly. Next, a lateral dissection of the last elements of the gastrocolic omentum should be completed, connecting to the mobilization achieved by the first dissection.

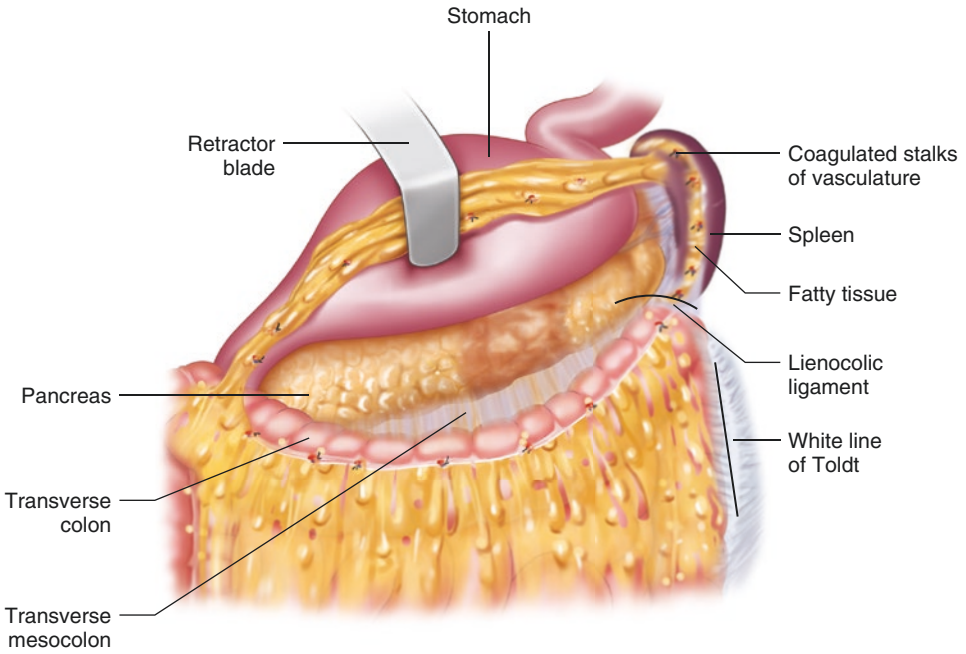
Figure 16.4

Dropping the splenic flexure of the colon. Dissection is performed along two fronts: (**1**) The interface of the lateral aspect of the colon is released along the "white line of Toldt" for a limited distance to allow for medial mobilization. (**2**) Lateral dissection of the last elements of the gastrocolic omentum is completed, connecting to the mobilization achieved in #1. Care should be taken to avoid injuring the colon and to control significant vascular stalks within the lienocolic ligament

Care should be taken to avoid injuring the colon and to control significant vascular stalks within the lienocolic ligament. Doing so can be particularly challenging in the face of sinistral hypertension from splenic vein occlusion induced by pancreatic pathology.

Once this layer is bisected, a second, deeper plane of transection in fatty tissue is often required so that the colon can be fully mobilized inferiorly. Usually this transection exposes a natural, areolar embryologic plane, but it may be interrupted by the pathology in the tail of the pancreas. At this point, the splenic flexure and more proximal transverse colon can be retracted inferiorly, usually with bulky laparotomy packs behind a deep malleable retractor. This retraction presents a trough inferior to the lower pole of the spleen, allowing some of the posterior and lateral attachments of the lienophrenic ligament to be carefully released.

Figure 16.4



16.2.5 Step 5: Dissection of the Pancreatic Body and Exposure of the Superior Mesenteric Vein

Dissection of the pancreatic body commences proximal to the area of pathology and proceeds medially towards the neck. The interface between the pancreas tumor and the base of the transverse mesocolon is released, as shown in Fig. 16.5. This natural embryologic plane is an extension of the lienocolic ligament. Care should be taken to avoid straying within the transverse mesocolon, which can be wafer-thin at times. Continue in this layer directly under the pancreatic neck to expose the anterior surface of the SMV. General landmarks include the termination points of the gastroepiploic and middle colic veins, which often coalesce into a common venous trunk. As depicted in Fig. 16.5, it is common to encounter a small, unnamed venous branch originating directly from the underside of the pancreatic neck and draining into the left side of the SMV. Though delicate (and often frustrating), this vessel must be managed in order to fully expose the portal vein canal and portosplenic confluence from this inferior approach.

Figure 16.5

Dissection of the pancreatic body and exposure of the superior mesenteric vein (*SMV*). General landmarks include the termination points of the gastroepiploic and middle colic veins. Dissection of the pancreatic body commences proximal to the area of pathology and proceeds medially toward the neck. The interface between the pancreas tumor and the base of the transverse mesocolon is released. It is common to encounter a small, unnamed venous branch (*star*) originating directly from the underside of the pancreatic neck and draining into the left side of the SMV. This delicate vessel must be managed in order to fully expose the portal vein canal and portosplenic confluence from this inferior approach

Before the next step of dissecting the portal canal, it is useful to obtain control of the pancreatic body. From the dissection plane just created, the pancreatic parenchyma can be fully lifted out of the retroperitoneum in an inferior-to-superior approach along this natural embryologic plane if it is not involved with infiltrative tumor or the effects of pancreatitis. This dissection plane is now posterior to the splenic vein, which at this position is virtually always enveloped within the pancreatic body. Deep (posterior) to this plane is the anterior aspect of Gerota's fascia. This is the dissection plane that is used to perform a splenorenal (Warren) shunt for relief of portal hypertension. Using manual elevation, the whole body of the pancreas can be encircled within the surgeon's hand. A window on the superior border of the pancreatic body can be dissected open (lateral to the previously developed splenic artery takeoff, yet above the meandering splenic artery in the retroperitoneum), and a Penrose drain can be placed around the pancreatic body (Fig. 16.6). This will facilitate the ultimate removal of the gland from the retroperitoneum once it is transected proximally. Obviously, pathology situated more proximally in the body of the pancreas may rule out this step at this point.

Figure 16.5

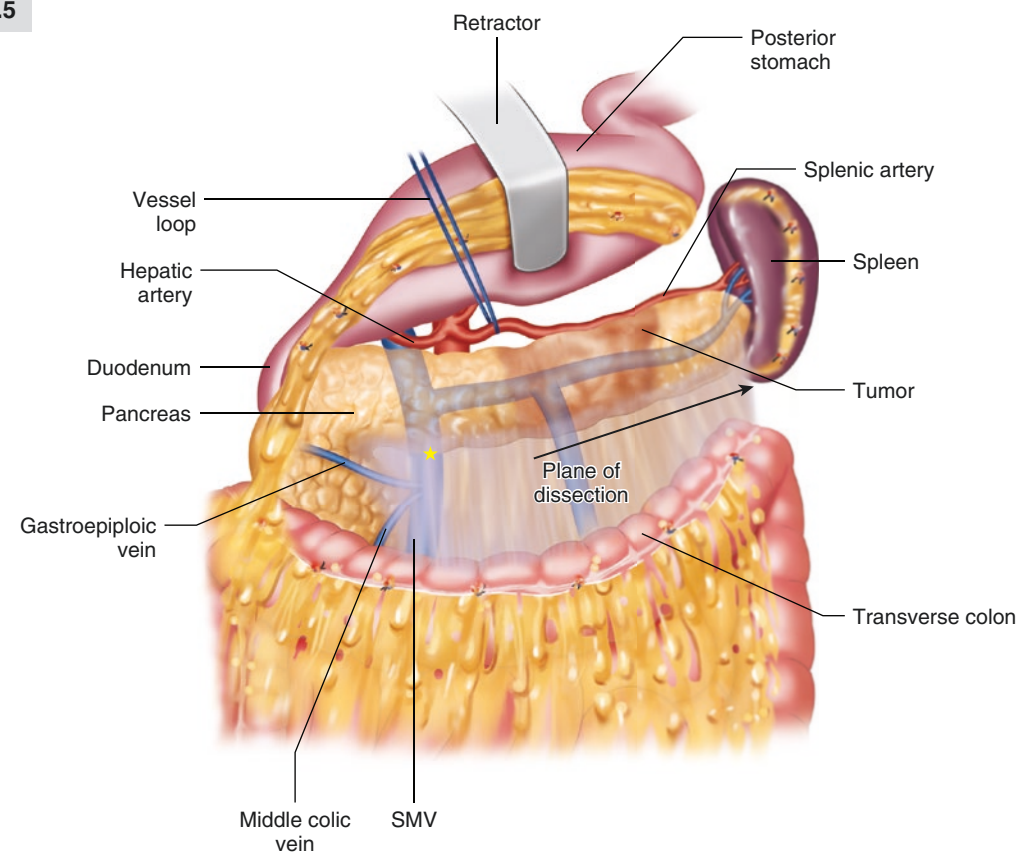
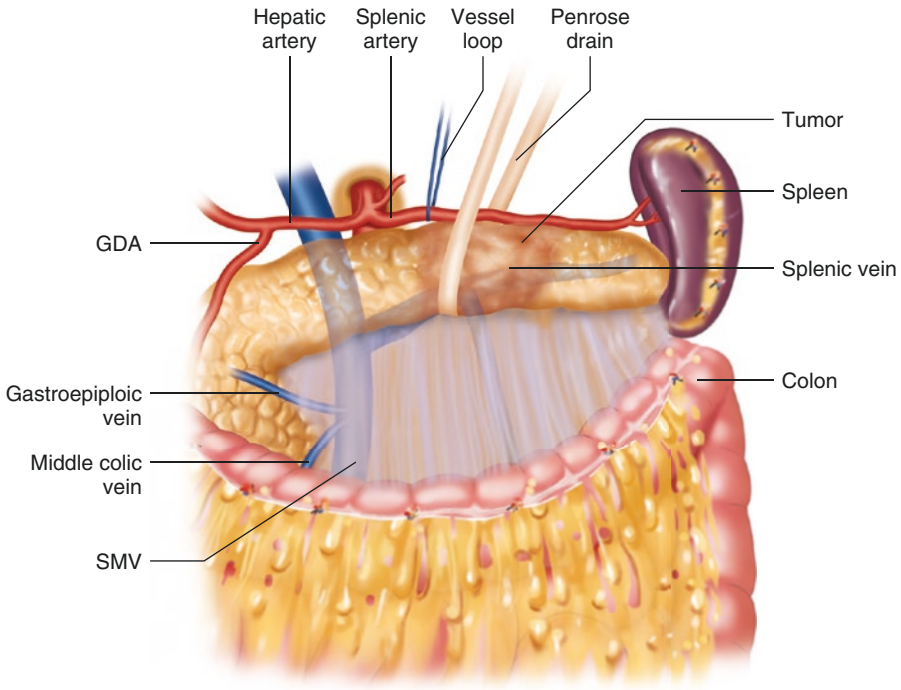


Figure 16.6

Control of the pancreatic body. From the dissection plane just created, the pancreatic parenchyma can be fully lifted out of the retroperitoneum in an inferior-to-superior approach, if it is not involved with infiltrative tumor or the effects of pancreatitis. Using manual elevation, the whole body of the pancreas can be encircled within the surgeon's hand. A window on the superior border of the pancreatic body can be dissected open, and a Penrose drain can be placed around the pancreatic body to facilitate the ultimate removal of the gland from the retroperitoneum once it is transected proximally

Figure 16.6


Hepatic artery
Splenic artery
Vessel loop
Penrose drain
Tumor
Spleen
GDA
Splenic vein
Colon
Gastroepiploic vein
Middle colic vein
SMV

16.2.6 Step 6: Developing the Portal Vein Canal and Portosplenic Confluence.

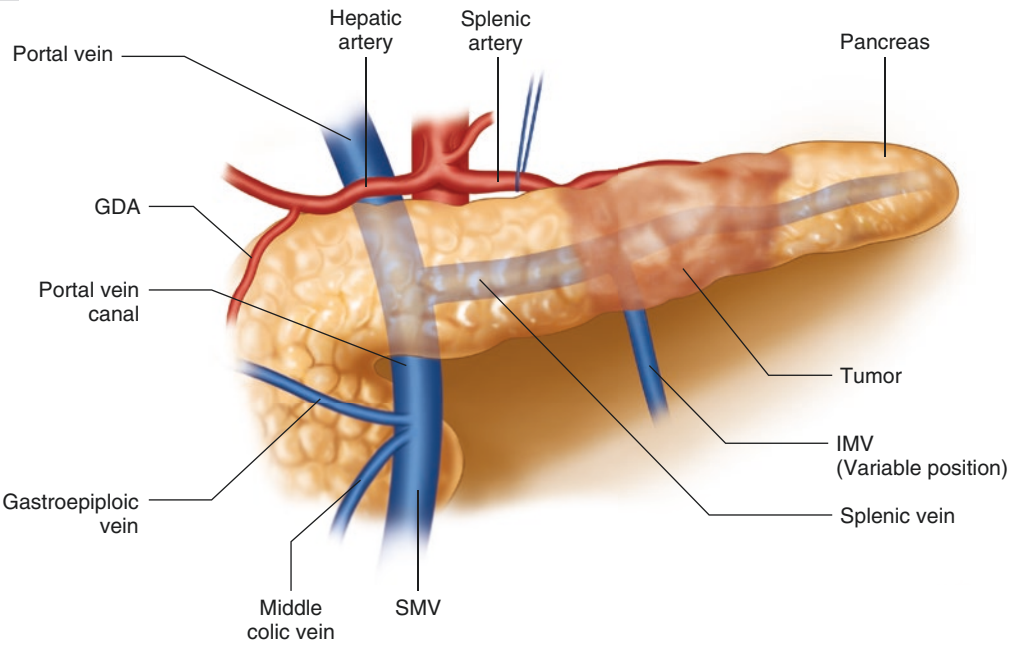
Lifting the pancreatic body from the retroperitoneum facilitates the identification of the portosplenic confluence (Fig. 16.7). In tracing the splenic vein medially back to this point, the inferior mesenteric vein (IMV) must be managed. Typically this drains directly into the splenic vein a few centimeters lateral to the confluence, and comes from deep within the retroperitoneal tissue. If so, it must be ligated in order to completely remove the body of the pancreas from the retroperitoneum. However, its insertion may be much closer to the confluence (within a centimeter of the SMV), or sometimes it enters directly into the confluence as a trifurcation. If so, it can be maintained.

Figure 16.7

Developing the portal vein canal and portosplenic confluence. Lifting the pancreatic body from the retroperitoneum facilitates the identification of the portosplenic confluence. Typically, the inferior mesenteric vein (*IMV*) drains into the splenic vein just lateral to the confluence and must be ligated, but if its insertion is close to or at the confluence, it can be maintained. The portal vein canal can be bluntly dissected anterior to the vein until the previous dissection plane on the superior border of the pancreatic neck is encountered

The portal vein canal can be dissected anterior to the vein using blunt dissection with the tip of a pediatric Yankauer suction device, or alternatively with spreading movements using a long Kelly clamp. In most cases, this will be a supple, virgin plane unaffected by pathology, and devoid of venous tributaries. Once the previous dissection plane on the superior border of the neck is encountered, the neck can be encircled with a vessel loop. Upward traction on the neck can then enable dropping the first few centimeters of the splenic vein off the pancreas, until the point where it becomes engulfed in the pancreatic body. Often, given that the posterior retroperitoneal plane behind the splenic vein has been developed, the splenic vein can be encircled at this point with another narrow vessel loop, but if this dissection is not easy, or if the exposure is awkward, this should be achieved after the pancreatic neck is transected.

Figure 16.7



16.2.7 Step 7: Transection of the Pancreatic Neck and Ligation of the Vasculature

Now that optimal vascular control has been established, transection of the pancreas can take place in a rapid, three-part sequence (Fig. 16.8). First, the splenic artery is ligated. This is a stout vessel that requires ligation with 2-0 silk. The stay side (originating off the celiac axis) should therefore be doubly controlled, and a suture ligature can provide more security. The inflow to the spleen has now been completely interrupted.

Next, the pancreatic neck should be transected. This is most conveniently achieved using a triple-rowed, dual-occlusion stapler (with or without reinforcement). The stapler should be deployed slowly and deliberately across the soft parenchyma so as not to crack the parenchyma or precipitate a hematoma. A thicker gland in the anterior-posterior plane requires a larger staple caliber (3 mm). Other

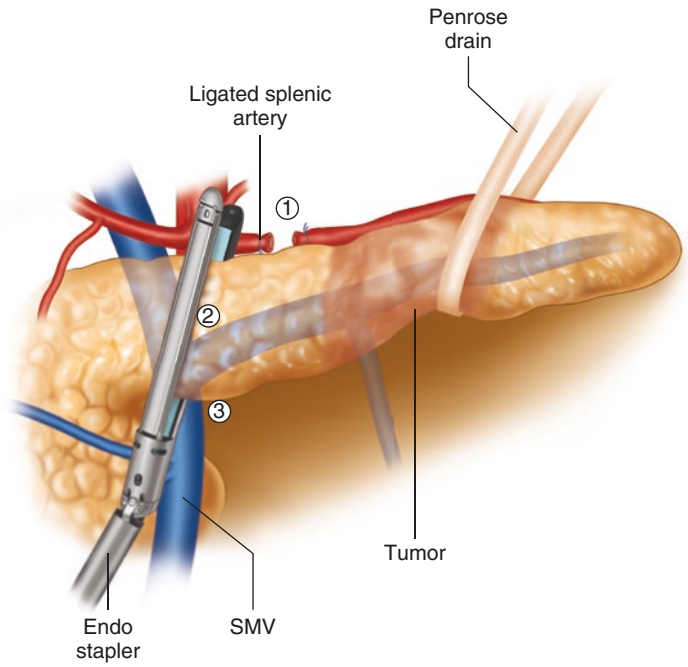
Figure 16.8

Transection of the pancreatic neck can be achieved in a three-part sequence: (***1***) The splenic artery is ligated, completely interrupting inflow to the spleen. (***2***) The pancreatic neck is transected. This figure shows the use of a stapler. (***3***) With full anterior exposure at its confluence with the portal vein, the splenic vein can now be mobilized, fully encircled, and safely ligated

approaches include transecting with a single-sided (TA) stapler if margin assessment may be of value. Alternatively, the gland can be transected by either knife or electrocautery, at the cost of greater blood loss, and the gland and pancreatic duct can be ligated directly. If margin involvement with either intraductal papillary mucinous neoplasm (IPMN) or malignancy would alter surgical decision making (i.e., completion pancreatectomy), a frozen section analysis can now take place.

Lastly, transection of the neck allows for full anterior exposure of the splenic vein at its confluence with the portal vein. The splenic vein should now be able to be mobilized for 3–4 cm laterally before it disappears into the parenchyma of the pancreatic body and can be fully encircled. Ensuring that the insertions of the coronary vein and IMV are free from this area, the splenic vein can be safely ligated, using a gray-load endovascular stapler.

Figure 16.8



16.2.8 Step 8: Retrograde Removal of the Distal Pancreas and Spleen

Once the pancreas is transected and vascular control has been achieved, the distal pancreas can be removed from the retroperitoneum in a retrograde (from medial to lateral) fashion (Fig. 16.9). Two 2-0 silk figure-of-eight sutures can be applied to the transected pancreas on the specimen side to facilitate upward traction and exposure. Because all major vasculature has been controlled, any bleeding incurred from the spleen or splenic vein is functionally inconsequential. Two planes of transection must be achieved simultaneously. The superior border of the pancreas must be freed off the retroperitoneum above the course of the often-meandering splenic artery. This plane contains numerous lymph nodes draining the tail of the pancreas back towards the celiac nodal basin. Care should be taken to avoid incursion into the adrenal gland, the only structure of importance in this deep zone. Finally, as the dissection proceeds further laterally, the posterior attachments of the spleen (lienorenal and lienophrenic ligaments) must be severed, which is most efficiently achieved using an energy coagulation device such as the LigaSure while the specimen is being lifted by traction away from the retroperitoneum. The specimen can now be removed from the abdomen and its margins marked for proper pathologic assessment.

16.2.9 Step 9: Final Considerations

The left upper quadrant should be investigated for hemostasis, particularly along the final transection plane of the lienorenal and lienophrenic ligaments. The greater curvature of the stomach should be reinspected, especially superiorly, at the high fundus, where transection of the final short gastric vasculature can often be performed under compromised visualization. The transection line of the pancreas and vasculature ligations should be revisited and hemostasis ensured. As mentioned in Step 1, a peritoneal patch can be attached to the transection line to potentially seal any retrograde leak [7].

Figure 16.9

Retrograde (medial to lateral) removal of the distal pancreas and spleen. Two planes of transection must be achieved simultaneously: The superior border of the pancreas must be freed off the retroperitoneum above the course of the splenic artery, and as the dissection proceeds further laterally, the posterior attachments of the spleen (lienorenal and lienophrenic ligaments) must be severed

The stalk of the umbilical ligament is coursed behind the antrum of the stomach through the previously opened gastrohepatic ligament. The peritonealized surface of this fatty appendage can be attached to the pancreatic transection line using a limited number of 2-0 silk sutures in a mattress fashion through the pancreatic parenchyma. Finally, a soft, externalized suction drain (such as a #19 Blake drain) can be placed through the abdominal wall and coursed above the splenic flexure of the colon, along the diaphragm, and across the dissection bed to lie close to the transection line.

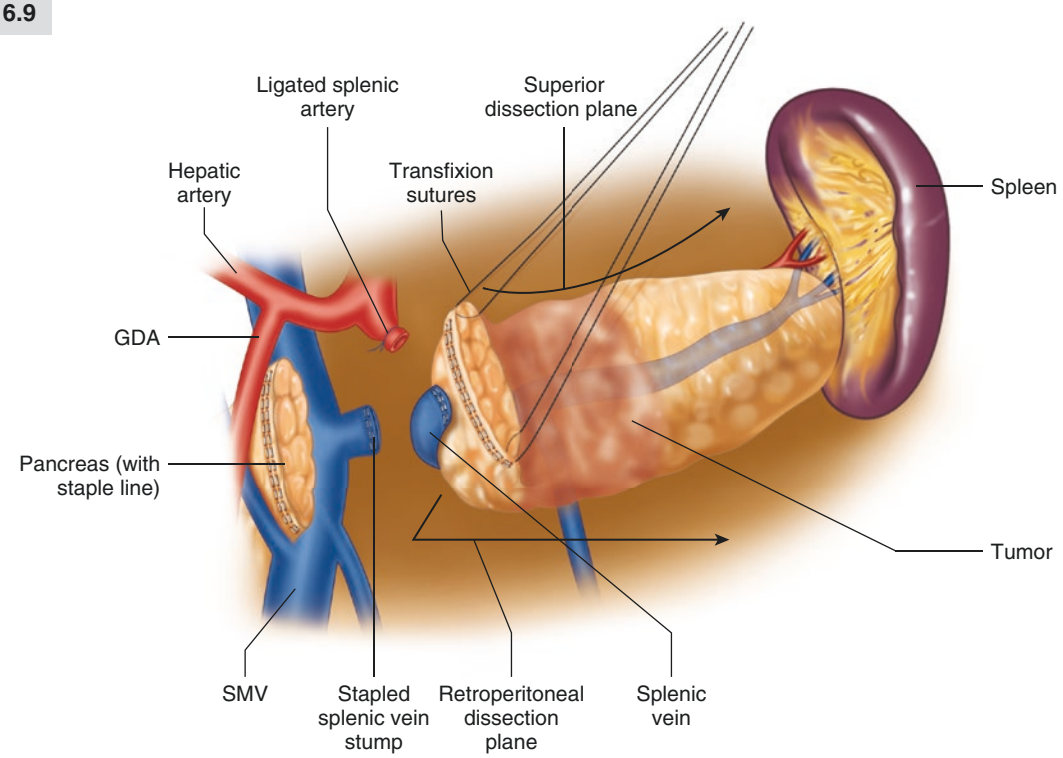
16.2.10 Technical Variations

Obviously, the natural resection planes described above may need to be altered to ensure clean margins around the pathology of interest. These changes may require incursion into Gerota's fascia or the mesentery of the transverse colon, or en bloc incorporation of portions of the stomach, colon, adrenal gland, renal vein, kidney, or diaphragm, as necessary.

Transection of the pancreas over the portal vein canal, as described here, is absolutely necessary if the pathology is situated proximally in the body of the gland. If the pathology is focused more distally, however, less pancreatic parenchyma can be resected. One option is transection of the midbody en masse with the splenic vasculature. The splenic artery can be focally isolated along the upper border of the gland for ligation. The splenic vein, embedded within the body, can be controlled with a single firing of a stapling device designed for thick tissue. Alternatively, select nonmalignant lesions (particularly small neuroendocrine tumors or cysts) can be situated within an intraperitoneal region (last 5 cm) of the tail. In this case, the last few centimeters of the tail can be "lifted" off the vessels of the splenic hilum and the parenchyma can be transected in isolation. This in essence becomes a spleen-preserving "tail-ectomy."

Splenic preservation can also be achieved through two other approaches: (1) The Warshaw technique preserves the vascular flow through the short gastric arcade [8]. The splenic artery and vein are transected in two places, proxi-

Figure 16.9



mally (as described here) and distally, at the splenic hilum. In this case, vascular load staplers are generally used to dissociate the distal pancreas from the spleen, and care must be taken to ensure that no residual pancreatic tissue remains. (2) In anatomically favorable circumstances, the full length of the splenic artery and vein can be dissociated from the pancreas and left in continuity with the spleen. Meticulous dissection is required, as the pancreas is supplied by numerous minute branches emanating from these vessels. Furthermore, these vessels are usually encapsulated within the pancreatic parenchyma (partially if not wholly) for long distances (up to 10 cm or more). This technique is associated with longer operative times and greater blood loss [9].

16.3 Discussion

Regardless of the technical approach used, DP is a major operation with a significant morbidity profile. The average hospital stay is generally about 5–7 days. The need for a reoperation should be less than 5%, usually for bleeding. Transfusions are required in about 10% of patients, and fewer than 10% require a stay in the intensive care unit. Complications mirror those of other major abdominal surgical procedures (i.e., wound infection, pulmonary embolism, pneumonia, myocardial infarction), with a frequency of about 1–5%. Rates of perioperative mortality are only about 1–2%, most commonly from late pulmonary embolism [10].

As is the case for Whipple resection, organ space infection is the primary complication of this procedure and similarly occurs at a rate of 20–40%. In the case of DP, postoperative pancreatic fistula (POPF) is the result of failure to adequately seal the pancreatic duct, the cut transection surface, or both. Interestingly, these leaks often manifest with infection, despite the fact that they do not involve an enteric anastomosis (as is the case with proximal resections). To manage this occurrence, most surgeons still place external drains during the operation and maintain them for a short term in the recovery period. Sometimes additional, percutaneously placed drains are required to manage local sepsis, but fortunately, these fistulas rarely result in reoperations, major long-term morbidity, or mortality.

To date, reliable predictors of POPF in DP have not been described in the literature. Effective fistula mitigation strategies have also been elusive, for both open and minimally invasive techniques. Neither somatostatin analogues (e.g., octreotide) nor anastomotic sealants (e.g., fibrin glue) have shown any value in decreasing POPF rates. Other approaches that have been proposed but not yet substantiated include energy ablation of the transection edge, pancreatic duct anastomoses to a Roux-en-Y limb, and transpapillary stenting of the ampulla of Vater (to decrease proximal ductal pressure). Controversy still abounds over whether the technique of parenchymal transection and duct occlusion matters. A recent randomized controlled trial showed no difference between stapled transection versus sharp transection with suture closure of the parenchyma and duct [11]. The value of staple-line reinforcements has thus far shown mixed results.

Prophylactic immunization against overwhelming postsplenectomy infection (OPSI) is recommended for those patients who have splenectomy associated with their DP. Ideally, the immunization should take place about 2 weeks before the operation, but this is generally impractical in clinical practice. However, as a process quality measure, it should be ensured that these patients receive vaccines against pneumococci, meningococci, and *Haemophilus influenzae* type b prior to their discharge from the hospital, and they should be vaccinated yearly against influenza. Choosing spleen preservation, or the specific technique of splenic preservation if performed, has not been shown to decrease the rate of OPSI, which is excessively rare. Furthermore, splenic preservation has not been associated with any appreciable perioperative benefit in any quality study to date [9]. Reactive thrombocytosis (>500,000 platelets/μL) is common after splenectomy (up to 75%), but clinical manifestations of thrombosis are actually rare (about 5%) and usually occur at levels of 600–800 × 10^3/μL. Though its true efficacy is not well studied, antiplatelet therapy (81 mg ASA daily) is recommended when platelet levels approach or exceed 750 × 10^3/μL, and certainly should be used when the level exceeds 1000 × 10^3/μL.

Long-term consequences of DP include glandular insufficiencies. As in the case of proximal pancreatic resections, new-onset diabetes occurs in up to a quarter of patients, and the rate may be higher on longer-term follow-up, which has been poorly studied. Similarly, exocrine insufficiency can result in steatorrhea, weight loss, and malnutrition in up to 25% of patients. Rates of these complications are likely to be related to the extent of gland removed. For these reasons, parenchyma-sparing options are available for certain pathologies with low malignant potential that are situated in the neck, body, or tail of the pancreas. These options include enucleation, segmental pancreatectomy, or modification of the plane of transection as noted above, but these methods often have higher perioperative morbidity, especially POPF.

Because most patients are undergoing DP for management of cystic neoplasms, neuroendocrine tumors, or other lesions of relatively low malignant potential, long-term survival is excellent. The prognosis is less optimistic for patients who undergoing DP for adenocarcinoma; their median survival is 1–2 years, and 5-year survival is roughly 15%. Just as with proximal resections for cancer, predictive factors for recurrence include tumor size and differentiation, lymph node involvement, and positive margins. The significance of positive margins underscores the importance of effective operative technique that adheres to proper oncologic princi-

ples, and may be improved by specific modifications of the basic procedure described here (*see* RAMPS [6]).

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Laparoscopic Distal Pancreatectomy

17

James J. Mezhir and James R. Howe

17.1 Introduction

Minimally invasive approaches to distal (left) pancreatectomy have been shown to produce equivalent short-term and long-term outcomes for the treatment of benign and malignant pancreatic diseases, including equivalent or better operative outcomes such as reduced blood loss, decreased pain medication requirements, and shorter hospital stay in retrospective studies from expert surgeons in high-volume centers [1–4]. Oncologically, lymph node retrieval, histologically negative margins, and recurrence have also been shown to be equivalent to open procedures in well-selected patients [3].

Pancreatic neuroendocrine tumors (PNET) represent a unique entity: they vary in location and can be small and therefore difficult to localize intraoperatively. Furthermore, many patients with PNETs have soft glands, and because these lesions do not typically cause pancreatic ductal dilatation, the risk for post-pancreatectomy pancreatic fistula is high [5]. Some of these characteristics render PNETs ideal for a laparoscopic approach to resection, however. It is important to note that the indications for resection of PNETs should not change based on the availability of minimally invasive technology.

Evaluation of a patient for distal pancreatectomy should include several considerations. As with any pancreatic malignancy, patients with PNETs require local and distant disease staging with high-quality cross-sectional imaging. Patients are first imaged with triple-phase, contrast-enhanced CT using a pancreas protocol technique with thin (2 mm) cuts. Distant disease is not a contraindication to resection, but it may alter the approach if a liver-directed procedure is required at the time of pancreatectomy [6]. Close proximity of the tumor to the takeoff of the splenic artery, retroperitoneal tumor invasion, or extensive lymphadenopathy are relative contraindications to laparoscopic distal pancreatectomy.

From a technical standpoint, some PNETs may be amenable to splenic preservation. Select tumors located in the body or tail of the pancreas without obvious lymphadenopathy may allow for pancreatectomy with preservation of the splenic artery and vein. If the splenic artery and vein must be resected because of tumor location or vascular invasion, the spleen may still be preserved with an intact short gastric arcade (the Warshaw procedure) [7]. Furthermore, based on the location and size of a PNET, an anatomic formal left pancreatectomy may not be required. Other procedures such as enucleation and central pancreatectomy are beyond the scope of this chapter but remain important technical procedures for the pancreatic surgeon treating patients with PNETs.

This chapter describes the technical considerations and approaches to laparoscopic distal pancreatectomy. The focus of the chapter is a total laparoscopic approach, but variations such as a hand-assisted technique and the technical aspects of splenic preservation are also addressed.

17.2 Laparoscopic Distal Pancreatectomy with Splenectomy

17.2.1 Patient Positioning and Port Placement

This operation can be performed in the right lateral decubitus position, supine, or in lithotomy. The choice of position is based primarily upon surgeon preference, ergonomic comfort, the patient's body habitus, and tumor location. We prefer the patient be positioned supine on a beanbag with straps over the legs and chest to allow for table movement, as steep reverse Trendelenburg with right lateral rotation often facilitates this procedure. In patients with a short distance between the xiphoid and the umbilicus, an infraumbilical 12-mm port

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J.R. Howe (ed.), *Endocrine and Neuroendocrine Surgery*, Springer Surgery Atlas Series, DOI 10.1007/978-3-662-54067-1_17

is placed using the Hassan technique to gain safe access to the abdomen. This incision can later be extended downward if necessary for specimen retrieval. The location of the operating surgeon is user-dependent and may change when training surgical house staff. The operating surgeon may also prefer to stand between the legs, positioned in lithotomy. When the operating surgeon is on the patient's right side, a 10- or 12-mm supraumbilical or infraumbilical port is placed to gain access into the peritoneum, and after insufflation, another 10–12-mm port is placed to the patient's left side at the level of or above the umbilicus. This port will be used by the assistant, who will help retract to expose as needed; these two ports of 10–12 mm will be used for the camera and staplers, although a 5-mm camera may also be used so that only one larger port is needed. The operating surgeon will place two additional ports (which can be 5-mm ports) on the patient's right side at or slightly above the level of the umbilicus, to be used for retraction and dissection. One port may be placed in the subxiphoid region for retraction of the liver and stomach, if necessary. The ports should be directed towards the midline and left upper quadrant, where most structures are located (Fig. 17.1).

It is important to note that there is not a uniform way to position or place ports for every patient. We have found in our experience that there is some variability depending on the type and location of the tumor, the patient's body habitus, and the experience of the operative assistant. Also, some maneuvers may be completed by a team approach involving the surgeon and the assistant, often based on the best visual and ergonomic angle. The ultimate goal is to have a comfortable arrangement for both the surgeon and the assistant that facilitates a safe operation.

17.2.2 Dissection of Peripancreatic Structures

A 30° or 45° camera is introduced and the abdomen is explored systematically for the completion of operative staging. Then the patient is rotated to the right and placed in steep reverse Trendelenburg, and the splenic flexure is lowered using an electrothermal dissector (ultrasonic shears or electrothermal bipolar tissue sealing device). As the operation progresses, the lesser sac is entered and the omentum is separated from the greater curvature of the stomach (Fig. 17.2). The stomach is grasped and held up to expose the plane of dissection for the operating surgeon. If the short gastric vessels are to be divided, take care to completely encompass these vessels with the electrothermal device to avoid partial transection, which can result in significant bleeding. When splenectomy is planned, the dissection is carried up to the fundus of the stomach to free the spleen completely from the stomach.

Once the greater curvature is freed, the stomach can be retracted out of the field under the left lateral segment of

Figure 17.1

Port placement for laparoscopic distal pancreatectomy. The initial site of entry, whether by the Hassan or Veress technique, is left to the discretion of the surgeon. A supra- or infra-umbilical port (1) should be carefully placed so it can either join or be far enough away from an upper abdominal hand port (2; if necessary). Secondary working ports are placed on the right for tissue manipulation and electrical dissection devices and for retraction if needed (3, 4). Ports on the left are for the camera and more retraction by the assistant (5). This operation can be performed with as few as four ports, but extra ports should be utilized if the operation requires them

the liver. The use of a fixed hand or liver retractor here can facilitate this retraction, which will free the left hand of the assistant. Now that the pancreas is exposed, the dissection begins with freeing of the inferior and superior borders of the pancreas (Fig. 17.3). The inferior border of the pancreas is carefully dissected out by dividing the overlying peritoneum with an electrothermal dissector. The pancreas is then lifted up bluntly with a grasper to facilitate further dissection and careful identification of vascular structures. Laparoscopic ultrasound can help identify small PNETs if necessary to assist with determining the point of parenchymal division, which should be approximately 2 cm proximal to the tumor [8]. Inferiorly, the transverse mesocolon is lowered either laterally from the splenic flexure or medially at the point of transection, using a combination of careful blunt and bipolar dissection. Take care to dissect behind the pancreas carefully, which will allow visualization of the superior mesenteric vein (SMV), inferior mesenteric vein (IMV), and splenic vein (Fig. 17.4). This maneuver is not necessarily performed to assess resectability, but rather to allow these structures to be identified and protected during further dissection and transection of the pancreas. The SMV can be found anatomically by tracing the right gastroepiploic and/or middle colic veins superiorly.

While freeing the inferior border of the pancreas by lowering the transverse mesocolon, take care to identify the IMV to avoid inadvertent injury. Further dissection posteriorly and superiorly will expose the splenic vein. If the pancreas is going to be divided far left of the SMV *en masse* with the splenic vein, then SMV dissection is not necessary; this decision is dictated by tumor location and pathology. If a formal left pancreatectomy is planned, the dissection is carried medially until the SMV is reached, and then dissection continues under the pancreas while the SMV is freed and protected. At this point in the dissection, the venous structures are fully identified and ready to be divided.

The goal of the dissection at the superior aspect of the pancreas is to identify the splenic and left gastric arteries and to completely free the lesser curvature of the stomach off of the pancreas. Injury to the coronary or left gastric vein during this part of the operation can lead to severe hemorrhage and must be avoided. Identify the splenic artery, which most commonly arises superiorly off of the celiac axis; it is often tortuous and should not be confused with the hepatic artery takeoff (Fig. 17.5). It is important to have the patient's cross-sectional imaging available to help correctly identify vascular structures and the relationship of these structures to the tumor. The splenic artery does not have to be isolated at the takeoff unless there is concern for proximity of the tumor to the celiac axis. Once the splenic artery is confirmed, it can be taken more distally, when coursing superiorly along the pancreatic parenchyma. The vessel is freed in order to facilitate stapler placement, completing the dissection of the pancreas and major vascular structures.

Figure 17.1

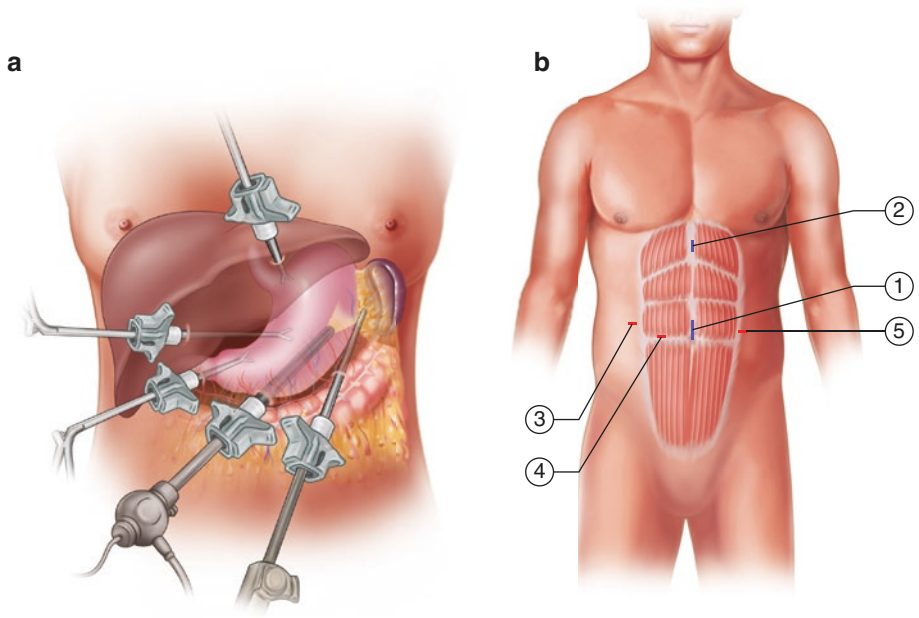


Figure 17.2

Exposure of the pancreas. With the stomach held up to the right and the omentum held inferiorly, the lesser sac is entered. With the patient in reverse Trendelenberg, the omentum and transverse colon will fall as will the greater omentum. The omentum is taken up to the level of the fundus if a splenectomy is planned, allowing the stomach to be pushed out of the field under the left lateral segment. If splenic preservation is planned, stop at the level of the short gastric arcade and retract the stomach for exposure

Figure 17.3

The peritoneum along the inferior edge of the pancreas is dissected out using an electrothermal device. It is safer to begin laterally and move medially, being careful not to go too deep and injure the inferior mesenteric vein (*IMV*). Dissect carefully over the region of the middle colic vein (*MCV*), as the superior mesenteric vein (*SMV*) will be right below the MCV

Figure 17.2

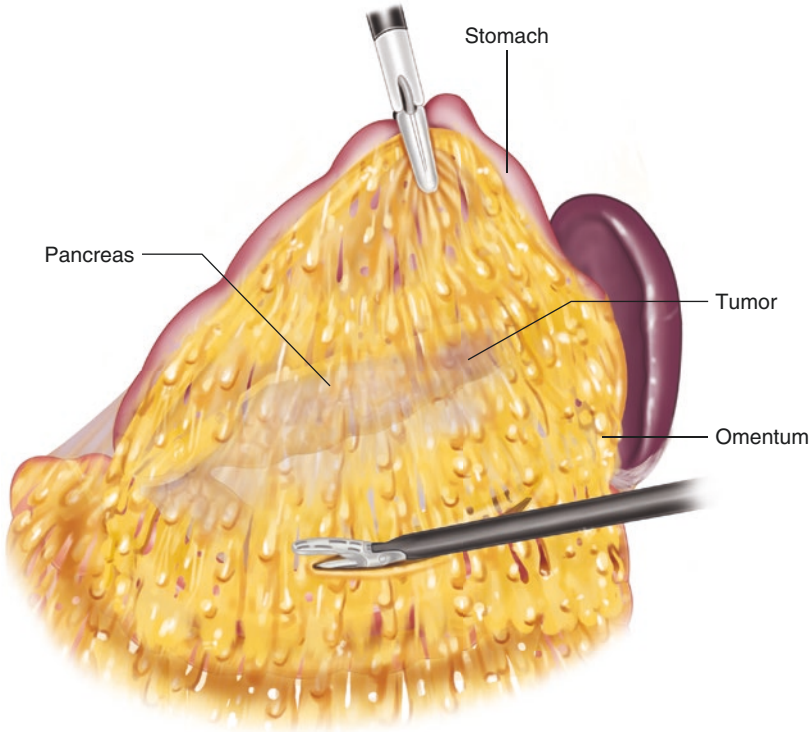


Figure 17.3

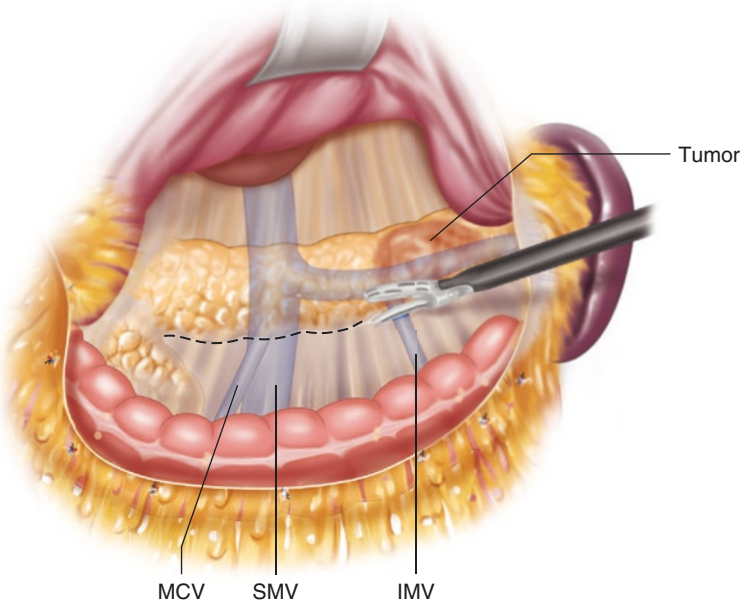


Figure 17.4

As the pancreas is exposed and freed from all attachments, critical vascular structures are identified. Dissection started inferiorly will expose the SMV by following the MCV and the right gastroepiploic vein. This maneuver also allows for exposure of the splenic vein, and it is important to confirm the anatomy before dividing any major vessels. The IMV can also be exposed as the inferior border of the pancreas is freed and transverse mesocolon is lowered. The IMV can be stapled or doubly clipped to facilitate dissection. Small branches from the splenic vein can be divided carefully with the bipolar device under direct vision. As the pancreas is freed inferiorly, dissection can continue behind the pancreas to free it from retroperitoneal attachments. Care must be taken to avoid injury to the renal vein and adrenal gland during this portion of the procedure. Moving laterally, the splenic flexure can then be freed from the spleen, and the entire pancreas is in view. This is a good time to perform intraoperative ultrasound if necessary

Figure 17.5

The top of the pancreas is freed from its attachments, taking great care to locate the splenic artery. Referring to the prior CT can confirm the artery's location, or intraoperative ultrasound can be used. It is critical to confirm celiac axis anatomy and its branches before any vessels are divided

Figure 17.4

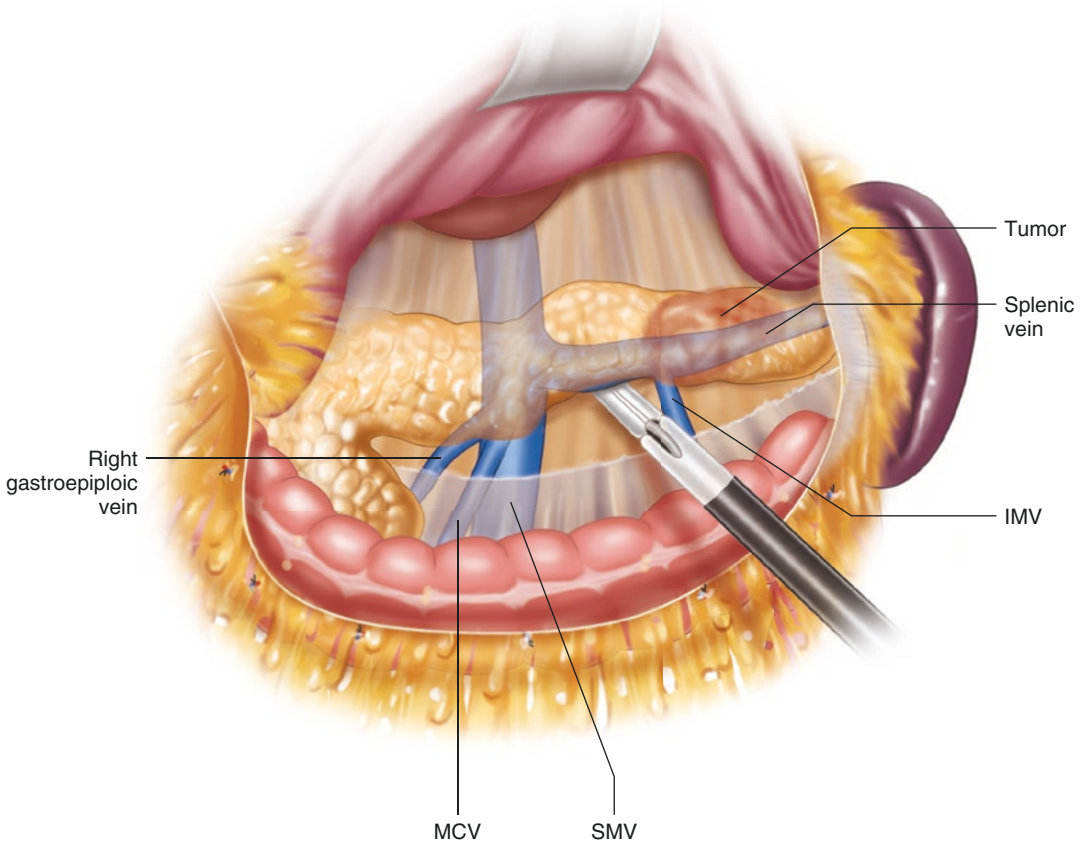
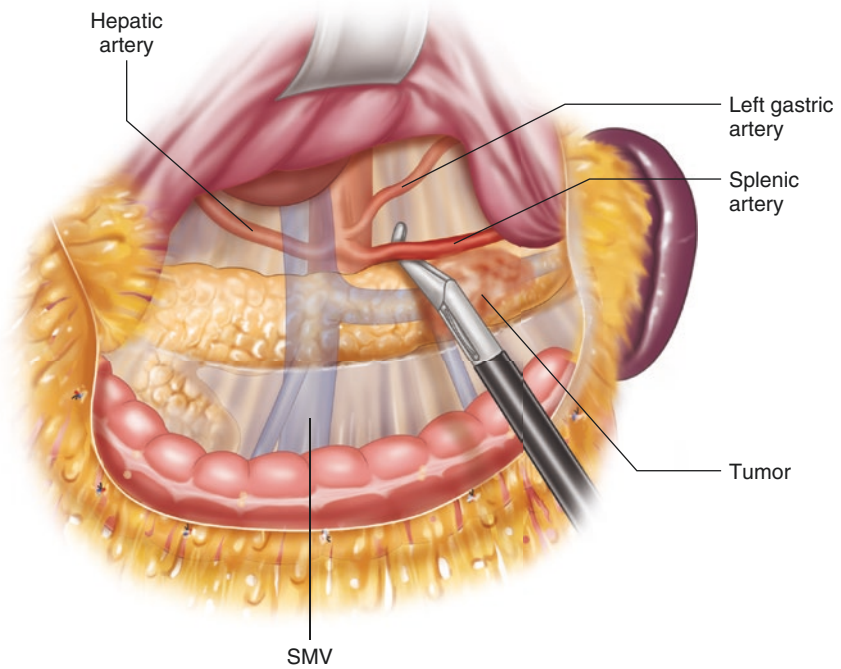


Figure 17.5



17.2.3 Division of the Pancreas and Vascular Structures

Now that the pancreas is completely mobilized, with the stomach, transverse colon, and mesocolon out of the field and the major vascular structures exposed and identified, the next step is to divide the vascular structures. The operation is technically easier to perform from a medial to lateral approach, which allows for protection of the major vascular structures and prevents bleeding from splenic traction. This approach also facilitates splenic preservation (see below). Once the desired point of transection is determined, divide the splenic artery first with an Endo GIA™ (Medtronic; Minneapolis, MN, USA) 30-mm or 45-mm stapler using a 2.5-mm load. The splenic vein is identified either within or below the pancreas, which will determine how the pancreas will be divided. When the splenic vein is firmly embedded in the posterior pancreas, *en masse* division to include both the pancreas and splenic vein may be preferred. An endo GIA™ 60-mm stapler using a reinforced purple load (three rows of staples, 3 mm, 3.5 mm, and 4 mm) or a reinforced black load (three rows of 4 mm, 4.5 mm, and 5 mm) is preferred for this division.

For separate division of pancreas and vascular structures, both the artery and vein must be fully exposed. If the splenic vein can be separated from the pancreas, then the pancreas is

Figure 17.6

Once the splenic artery has been divided with an Endo GIA™ stapler, and the vein location is confirmed, the pancreas is freed inferiorly from the retroperitoneum. Now the stapler is placed across the pancreas, positioned carefully behind the splenic vein if the pancreas and vein are to be taken *en masse*. Alternatively, the pancreas can be dissected out separately and stapled, and then the splenic vein is divided with a stapler

transected using an endo GIA™ 60-mm stapler with a purple or black load. At this point, the splenic artery can be divided with an endo GIA™ 2.5-mm load, and then the splenic vein is taken in similar fashion (Fig. 17.6). Now blunt dissection can be used to roll the pancreas and vessels laterally. The IMV will need to be ligated (stapled or clipped) as it enters into the inferior aspect of the splenic vein (Fig. 17.7). The pancreas is then carefully dissected off until the spleen is reached. Next, the splenic attachments to the lateral peritoneum are divided, as well as all of the short gastric vessels, and the spleen is completely freed. The specimen is placed in a large Endo Catch™ pouch (Covidien) and pulled into the 12-mm port. The incision is enlarged to facilitate removal. Morcellization of the spleen is not advised when the operation is being performed for malignancy.

This approach may vary with larger tumors, or perhaps if a patient has a splenic vein that is invaded and thrombosed on preoperative imaging. In these cases, after medial division of the pancreas, the splenic artery should be carefully dissected out proximally and divided with an endo GIA™ 2.5-mm load. One needs to beware of collateral vessels, as varices will form after splenic vein thrombosis, which can lead to troublesome bleeding. The splenic vein should be likewise divided, either after dissecting it out separately or, in most cases of advanced disease (with splenic vein thrombosis), in conjunction with dividing the pancreas.

Figure 17.6

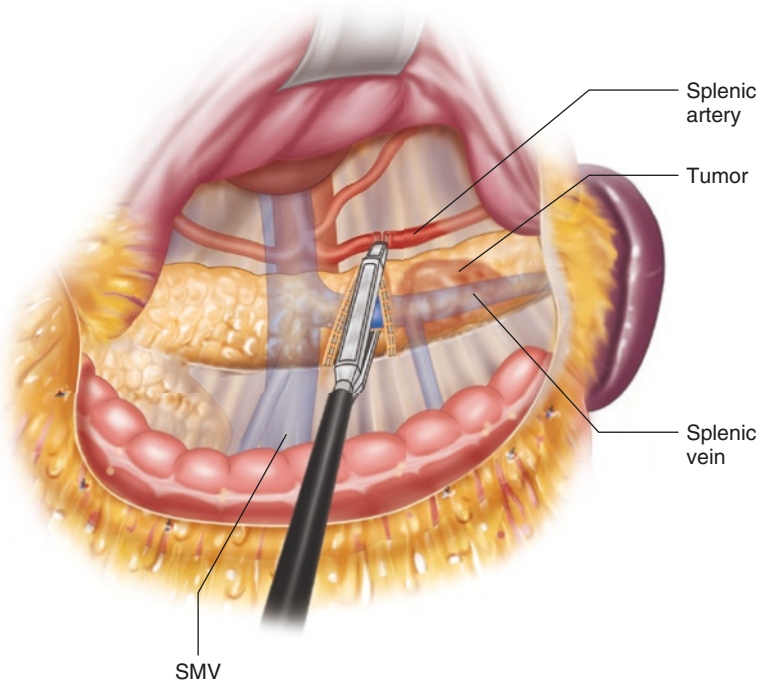
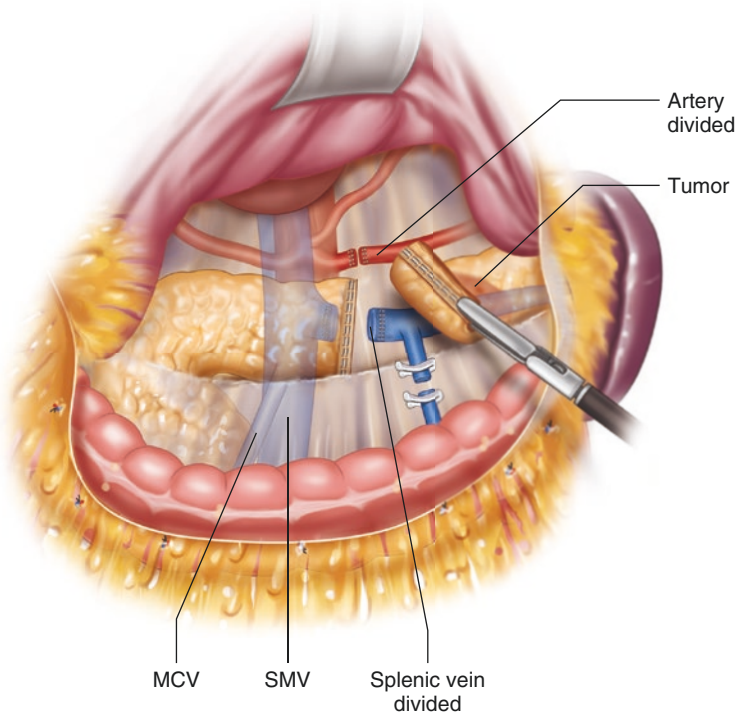


Figure 17.7

The pancreas is rolled laterally, exposing the IMV, which is divided between clips. The tissue superior to the splenic artery is divided with an energy device, keeping the splenic artery nodes with the specimen. The peritoneal attachments of the spleen are taken, freeing up the specimen

Figure 17.7



17.3 Laparoscopic Distal Pancreatectomy with Splenic Preservation

If splenic preservation is planned, then both the splenic artery and vein are left intact, and the pancreas is carefully rolled laterally. Branches coming off both vessels must be carefully identified and clipped or divided with an electrothermal device. Dissection is carried out all the way to where the pancreas ends near the spleen, and the pancreas is removed in an Endo Catch™ bag when it is completely cleared of these vessels. In many cases, the tumor will invade the splenic vein, and the splenic artery and vein therefore need to be divided. The spleen may still be preserved in these patients as long as the short gastric vessels are preserved (Warshaw procedure; Fig. 17.8). This approach has a very low risk for long-term complications and therefore can be considered in select cases [7]. The concept is that if the splenic vessels are to be taken because of the tumor location, then the spleen will receive its blood supply from the short gastric vessels. For this approach, the dissection along the greater curvature stops before reaching the short gastric arcade. It is important not to injure the

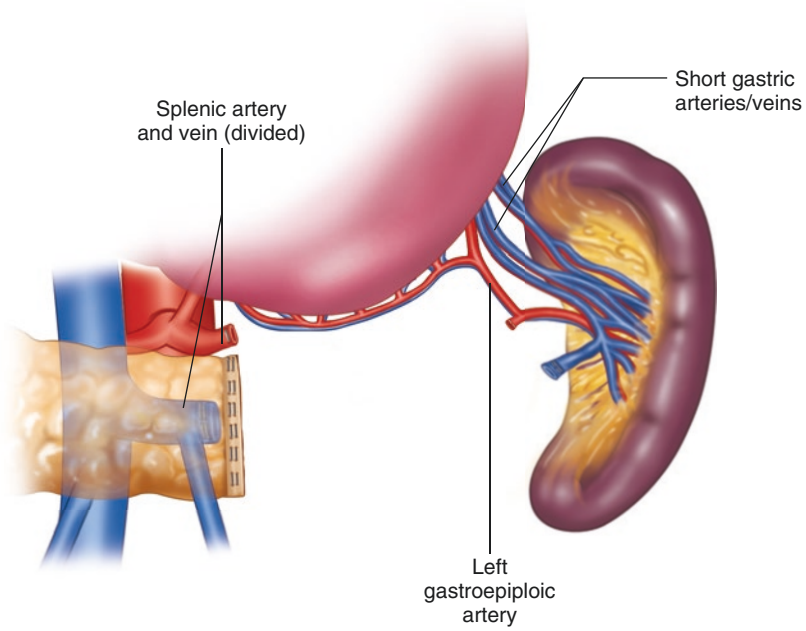
Figure 17.8

Warshaw procedure, with division of the splenic artery, vein, and pancreas proximally. Distally, the splenic artery and vein are taken near the hilum, preserving the short gastric vessels to the stomach for collateral flow

gastroepiploic vessels while freeing the stomach, as these will be the source of important collateral flow. The remaining maneuvers of this pancreatic resection remain the same as described, with division of the artery, vein, and pancreas proximally. When the end of the pancreas is reached, dissection and ligation of the splenic artery and vein branches are carefully carried out proximal to the splenic hilum. These vessels are then divided separately or together with an Endo GIA™ vascular 2.5-mm staple load to complete the dissection. The spleen is left behind, and the pancreas is placed into an Endo Catch™ bag and removed through a 12-mm port; the site may need to be enlarged to accommodate a larger specimen.

After removal of the specimen, inspect for hemostasis along the vessels and in the retroperitoneum. Bleeding from the spleen (if preserved) can be dealt with using the argon beam coagulator. Closed suction drainage is optional; many feel that it is important, but others use a selective approach based upon the risk for pancreatic leak. Nasogastric suction is not required routinely. The fascia is closed with a 0 Vicryl suture for all 10–12-mm trocar sites, and then the skin is closed with 4-0 absorbable sutures.

Figure 17.8



17.4 Hand-Assisted Laparoscopic Distal Pancreatectomy

Most cases can be performed with a total laparoscopic approach, but when there is difficulty, a hand port can facilitate the dissection, allow for palpation of vessels and other critical structures, and facilitate specimen removal. The hand port can be placed as an upper midline incision or in the right lower quadrant. The operating surgeon uses the left hand and the right hand holds electrothermal devices and staplers.

17.5 Pearls and Pitfalls

Positioning is a critical aspect of this operation, and reverse Trendelenburg with rotation to the right will facilitate the procedure. During the course of dissection, one of the key elements is to avoid inadvertent vascular injury. This includes tearing or injury to the major veins, including the SMV, IMV, and left gastric vein, or inadvertent division of the hepatic or left gastric artery. Short gastric vessels should be controlled carefully, as injury or partial division can result in significant bleeding. These vessels should be secured with an electrothermal dissector or clips, because they can bleed postoperatively. Securing of the splenic artery before the splenic vein and prior to mobilization of the spleen can help reduce unnecessary bleeding. The use of the hand port is a viable option during a difficult pancreatectomy; it may prevent conversion to an open procedure and will facilitate specimen retrieval. If at any point during the operation there is loss of control, failure to progress, or surgeon discomfort, conversion to an open procedure with an upper midline or left subcostal incision should be performed.

17.6 Results and Conclusions

Mortality from distal pancreatectomy in large series of both open and laparoscopic approaches ranges from 0.3% to 3% [1, 9]. Despite low mortality rates, morbidity remains a significant problem following distal pancreatectomy; common complications include pancreatic fistula, leak, abscess, bleeding, reoperation, delayed gastric emptying, and infection [1, 9]. Prospective recording and grading of complications remains critical for accurate reporting of outcomes in both retrospective and prospective studies. Along these lines, pancreatic fistula rates following distal pancreatectomy range from 12% to 31% in large series; these rates tend to be higher than the rates for pancreaticoduodenectomy [1, 9]. The approach to parenchymal transection has been studied extensively both retrospectively and prospectively, and no particular technique has evolved as superior with regard to fistula prevention. The use of intraperitoneal drains remains controversial, although evidence points to at least a selective approach to drainage with early removal.

Oncologically, laparoscopic and distal pancreatectomy have been compared in retrospective studies and found to be equivalent with regard to nodal harvest, the rate of positive margins, and recurrence [3]. Several retrospective series have evaluated laparoscopy for the treatment of PNETs and found this approach to be safe and feasible in select patients [6, 10]. Overall, it is important that the indication for resection should not change based on having a minimally invasive option for treatment.

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Pancreatic Enucleation

18

Attila Nakeeb and Henry A. Pitt

18.1 Introduction

Enucleation of pancreatic lesions is an alternative to formal pancreatic resection (pancreaticoduodenectomy or distal pancreatectomy) for the management of select pancreatic neoplasms. Advantages of pancreatic enucleation include preservation of pancreatic endocrine and exocrine function, shorter operative times, less intraoperative blood loss, and a decreased rate of serious complications when compared with pancreatic resections. Disadvantages of pancreatic enucleation include the lack of a formal lymphadenectomy and a slightly higher rate of grade A pancreatic fistula.

18.2 Indications

Neuroendocrine tumors, side branch intraductal papillary mucinous neoplasms, mucinous cystic neoplasms, serous cystadenomas, solid pseudopapillary neoplasms, and lymphangiomas are all potentially amenable to pancreatic enucleation. Absolute contraindications for enucleation include the presence of malignancy or involvement of the main pancreatic duct. The most frequent indication for the performance of a pancreatic enucleation is a small, benign pancreatic neuroendocrine tumor (PNET). Tumor factors important in selecting appropriate patients for enucleation include the size of the tumor (<3 cm), a low Ki-67 index or mitotic rate, and the absence of lymph node metastasis. In addition to size, there are several other considerations related to PNETs:

- Is the tumor functional or nonfunctional?
- Is the tumor sporadic or part of a multiple endocrine neoplasia syndrome?
- Is the tumor solitary or multiple?
- Is the tumor isolated or associated with liver metastases?

In general, functional tumors present when they are smaller, so they may be more amenable to enucleation. Similarly, sporadic, solitary, nonmetastatic tumors may be more appropriate for enucleation. Recently, several authors have advocated pancreatic enucleation also for the treatment of small, benign cystic neoplasms of the pancreas. For all tumors potentially amenable to pancreatic enucleation, proximity to the main pancreatic duct and location in the tail of the pancreas are considered relative contraindications.

18.3 Diagnostic Imaging

Helical (spiral) CT is the preferred noninvasive imaging test for pancreatic diseases. Helical CT scanning can delineate the anatomy of the pancreas and the surrounding organs in considerable detail, and can easily define pancreatic calcifications, inflammation, necrosis, and masses. Thin cuts are obtained through the pancreas and the liver during both the arterial phase and the venous phase after the injection of intravenous contrast dye. In addition to determining the primary tumor size, CT can also identify and evaluate invasion into local structures or metastatic disease. MRI and magnetic resonance cholangiopancreatography (MRCP) can be useful for defining the relationship between the pancreatic lesion and the pancreatic duct noninvasively.

Endoscopic ultrasound (EUS) plays an important role in the evaluation of pancreatic diseases. This semi-invasive test can be performed with a very low rate of complications (<0.1%). The particular strengths of EUS in the diagnosis of pancreatic neoplasms include its ability to (1) clarify small (<2 cm) lesions when CT findings are questionable or negative, (2) detect malignant lymphadenopathy, and (3) guide fine-needle aspiration (FNA) for definitive diagnosis and

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J.R. Howe (ed.), *Endocrine and Neuroendocrine Surgery*, Springer Surgery Atlas Series, DOI 10.1007/978-3-662-54067-1_18

staging [1]. Somatostatin receptor scintigraphy (SRS) utilizing a somatostatin analogue labeled with a radioisotope can be used to rule out distant metastatic disease in select patients with neuroendocrine tumors.

18.4 Patient Preparation

Every patient considered for a pancreatic resection needs a full evaluation of cardiac, pulmonary, and renal function. A complete array of laboratory tests must be obtained, including a complete blood count, renal panel, and liver panel. A nutritional assessment must be made to ensure that the patient can undergo surgery safely. If the patient has severe weight loss or an albumin less than 3 g/dL, strong consideration of supplemental nutrition is indicated. Serum tumor markers, including carcinoembryonic antigen (CEA) and CA19-9, are usually measured in patients with both solid and cystic tumors. If a neuroendocrine tumor is suspected by history (symptomatic), imaging (hypervascular on CT scan), or on preoperative biopsy, then serum levels of chromogranin A, insulin, proinsulin, glucagon, gastrin, vasoactive intestinal peptide (VIP), or pancreatic peptide (PP) should be measured as appropriate.

For lesions involving the body and tail of the pancreas, the patient should receive vaccination against encapsulated organisms to prevent post-splenectomy sepsis. These vaccines include *Streptococcus pneumoniae*, *Neisseria meningitidis*, and *Haemophilus influenzae*. The vaccines should be administered 1 or 2 weeks prior to the operation, if possible.

Figure 18.1

Exposure of the body and tail of the pancreas

Pancreatic enucleation is a "clean" operation, so preoperative administration of a first-generation cephalosporin is adequate antibiotic prophylaxis. As the operative time for enucleation is less than for resection, antibiotic redosing intraoperatively is seldom necessary.

18.5 Operative Technique

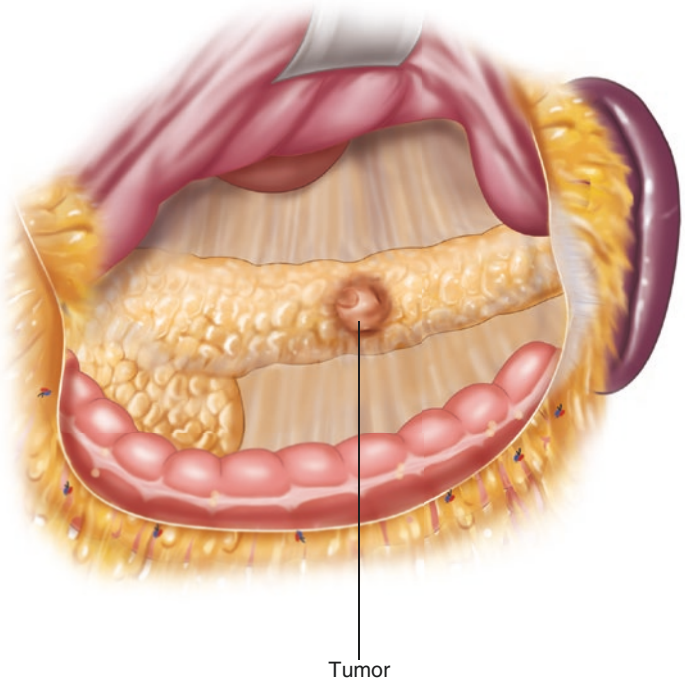
The first decision is whether to use an open approach or perform a minimally invasive operation. This choice will be based on surgeon expertise, patient preference, and the location of the lesion. In general, tumors or cysts that are anterior to the pancreas will be more amenable to enucleation. Lesions that lie posteriorly in the head and/or uncinate also can be enucleated, but an extensive Kocher maneuver is required.

18.5.1 Open Pancreatic Enucleation

18.5.1.1 Exposure of the Pancreas (Body and Tail)

An upper midline incision is used to gain access to the peritoneal cavity. Alternatively, a bilateral subcostal incision may also be used. Once the abdomen is entered, a careful exploration is performed of the liver and peritoneal surfaces to confirm the absence of disseminated disease. The lesser sac is entered by dividing the greater omentum just outside the gastroepiploic arcade (Fig. 18.1). Alternatively, the greater omentum may be taken off the transverse colon and be left attached to the greater curve of the stomach. Any adhesions between the posterior wall of the stomach and the pancreas are divided sharply to completely expose the body and tail of the pancreas.

Figure 18.1



18.5.1.2 Exposure of the Pancreas (Head and Uncinate)

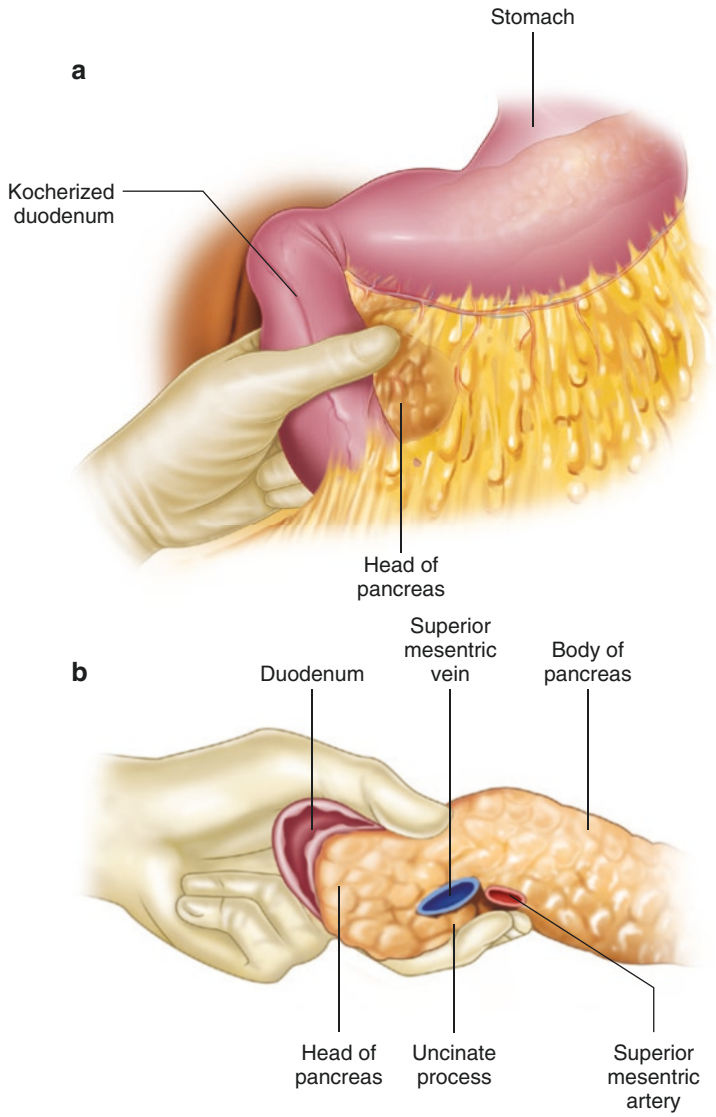
After gaining access to the peritoneal cavity, the hepatic flexure of the colon is mobilized and reflected inferiorly to expose the head of the pancreas and the duodenum. A complete Kocher maneuver is performed, elevating the head of the pancreas out of the retroperitoneum (Fig. 18.2). To maximize exposure of the pancreas, it is often

Figure 18.2

(**a**) A Kocher maneuver is performed to elevate the head of the pancreas out of the retroperitoneum. (**b**) Palpation of the head and uncinate process of the pancreas

necessary to divide the right gastroepiploic vein as it enters the superior mesenteric vein. Dividing this vessel connects the dissection of the head with the body and tail allowing for complete exposure of the anterior surface of the pancreas.

Figure 18.2



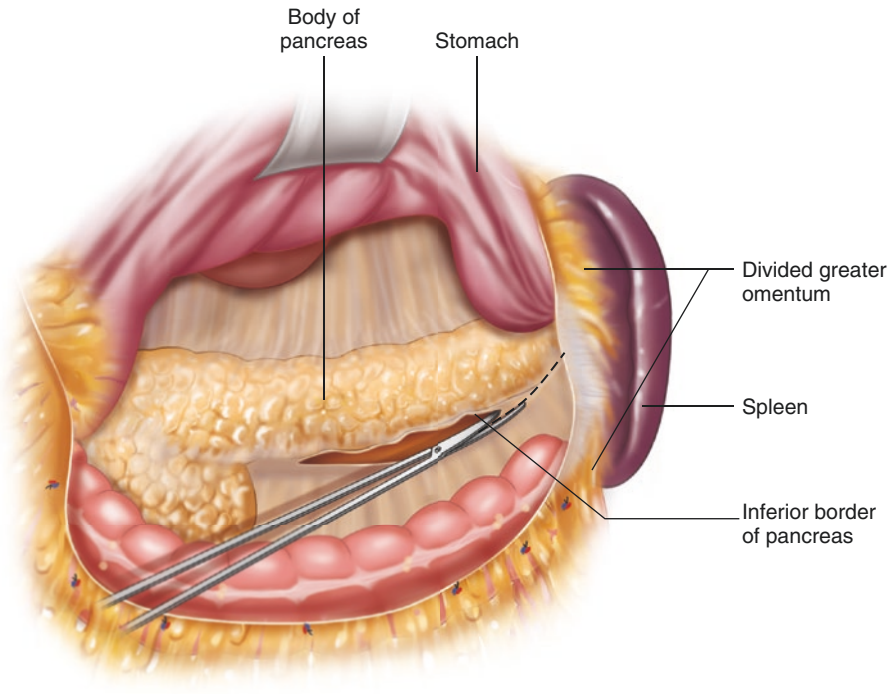
18.5.1.3 Mobilization of the Pancreas

Once the pancreas is completely exposed, the peritoneum on the inferior border of the pancreas is sharply incised (Fig. 18.3), and the pancreas is lifted out of the retroperitoneum. Caution should be taken to avoid any injury to the splenic vein, inferior mesenteric vein, or superior mesenteric vein.

Figure 18.3

The peritoneum on the inferior border of the pancreas is sharply incised

Figure 18.3


Body of pancreas
Stomach
Divided greater omentum
Spleen
Inferior border of pancreas

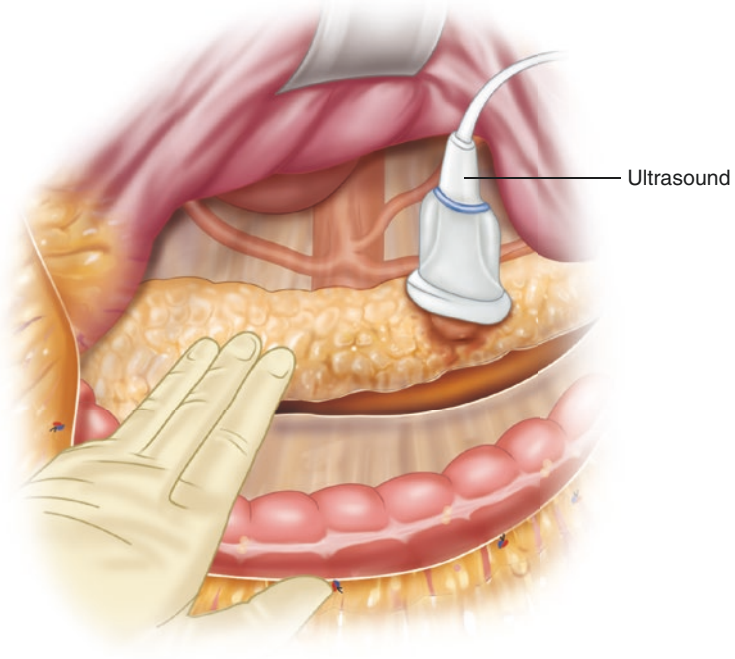
18.5.1.4 Bimanual Palpation and Ultrasound

The pancreas can now be palpated bimanually to identify any tumors. Intraoperative ultrasound imaging of the pancreas can be performed (Fig. 18.4) to localize nonvisible lesions and to further assess the relationship of the tumor to the main pancreatic duct. If concern exists that enucleation will result in injury to the main pancreatic duct, a formal pancreatic resection should be considered.

Figure 18.4

Intraoperative ultrasound imaging of the pancreas

Figure 18.4



18.5.1.5 Enucleation of Pancreatic Tumor

To proceed with enucleation of a deep lesion, the pancreatic parenchyma overlying the tumor should be carefully opened, with small vessels being ligated with fine sutures or cauterized (Fig. 18.5). Most lesions that are amenable to enucleation are on or close to the surface of the pancreas. A combination of sharp and blunt dissection is used to shell the tumor out of the pancreatic parenchyma. Small vessels are

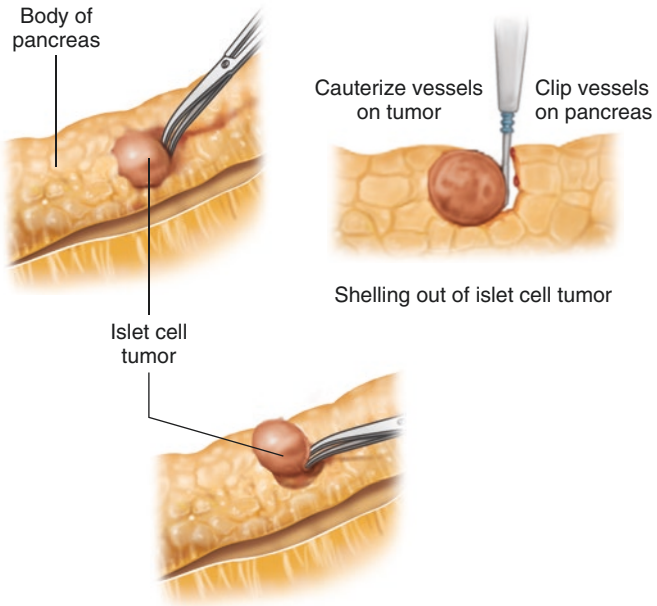
Figure18.5

Shelling out an islet cell tumor from the pancreatic parenchyma

controlled with a combination of fine sutures, clips, or an energy device. Dissection is begun at the edges of the lesion and continues with care being taken to stay close to but not entering the tumor.

Once the tumor is excised, the bed of the tumor should be carefully examined for any evidence of a major pancreatic duct injury. A closed suction drain should be left near the resection bed.

Figure 18.5



18.5.2 Laparoscopic Pancreatic Enucleation

18.5.2.1 Positioning and Port Placement

Tumors located in the body or tail of the pancreas or the anterior head of the pancreas may be considered for a laparoscopic approach. For lesions in the head, uncinate, or neck of the pancreas, the patient is positioned supine. For lesions located in the body or tail of the pancreas, the patient is placed in a semilateral (30°–45°) position with the left side up. The surgeon and the camera operator stand on the

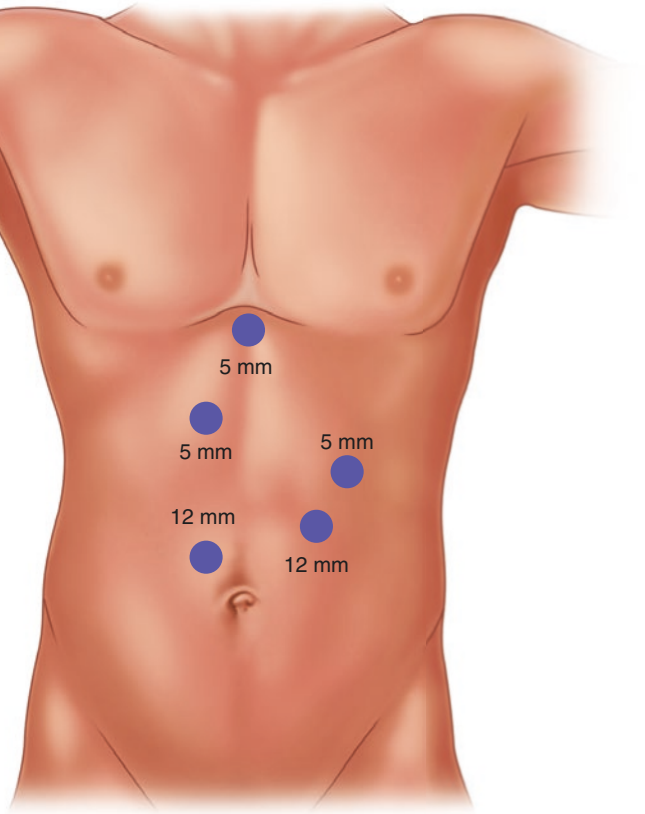
Figure 18.6

Port placement for laparoscopic pancreatic enucleation

patient's right side; the first assistant and the scrub nurse stand on the patient's left side.

Five ports are placed (Fig. 18.6) and a 10-mm 30° laparoscope is used. As in all pancreatic procedures, the peritoneal surfaces, the omentum, the mesentery, and the viscera should all be carefully inspected to rule out metastatic disease. Intraoperative ultrasonography may be employed to evaluate the liver and locate the lesion in the pancreas.

Figure 18.6



18.5.2.2 Exposure and Mobilization of the Pancreas

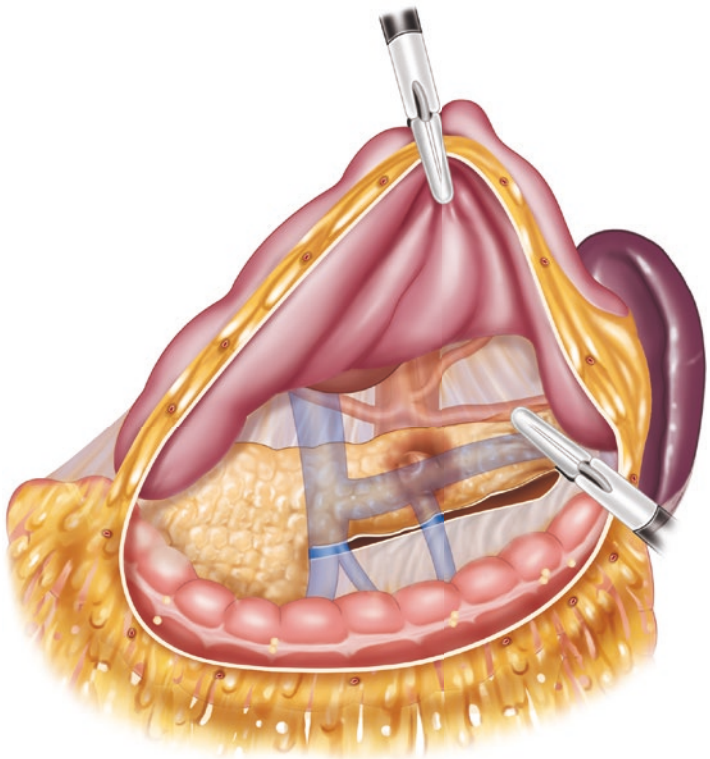
The pancreas is exposed by opening the lesser sac by dividing the gastrocolic omentum outside the gastroepiploic vessels. A retractor is advanced into the lesser sac through the subxiphoid port and used to elevate the stomach anteromedially (Fig. 18.7). Alternatively, the stomach can be sutured to the anterior abdominal wall with a temporary suture to obtain exposure.

Figure 18.7

The stomach is elevated anteromedially

After exposure of the pancreas, the peritoneum is incised along the inferior pancreatic border, and the pancreatic body is separated from the retroperitoneum by means of sharp and blunt dissection along its inferior border. Laparoscopic ultrasonography and direct visual inspection, combined with the findings from preoperative imaging, may be employed to determine the extent of the dissection.

Figure 18.7



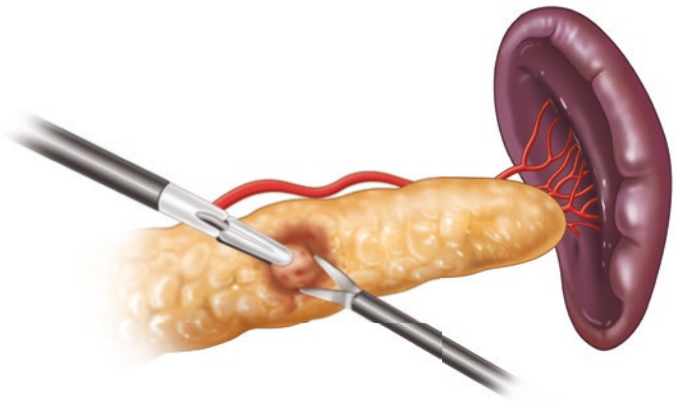
18.5.2.3 Enucleation

The lesion can then be dissected out of the pancreatic parenchyma using the ultrasonic shears and electrocautery (Fig. 18.8). The specimen is placed in a specimen retrieval bag and removed. The enucleation bed is then inspected for hemostasis and a closed suction drain is placed to control any potential pancreatic leak.

Figure 18.8

The lesion is dissected out of the pancreatic parenchyma using ultrasonic shears and electrocautery

Figure 18.8



18.6 Results

The enucleation of pancreatic tumors has been shown to be associated with a low operative mortality rate secondary to the limited dissection required and the lack of any reconstruction. In an analysis of the American College of Surgeons–National Surgical Quality Improvement Program (ACS-NSQIP) database, the odds ratio of mortality for enucleation was only 0.10 ($p < 0.01$) when compared with pancreatoduodenectomy, and 0.17 ($p < 0.01$) when compared with distal pancreatectomy [2].

Overall perioperative morbidity for pancreatic enucleation ranges between 40% and 60%, which is similar to the rate of morbidity for formal pancreatic resections. The most frequent complication that occurs with pancreatic enucleation is the development of a pancreatic fistula. The fact that the pancreatic parenchyma is normal in the vast majority of patients undergoing enucleation explains why 30–40% of these patients develop a pancreatic fistula. In comparison, when these patients undergo resection, a pancreatic fistula occurs in 25–30%, but it is more likely to be a clinically significant grade B or C fistula as defined by the International Study Group for Pancreatic Fistula classification. Though the rate of pancreatic fistula rate is high after enucleation, most are grade A fistulas with little clinical consequence.

Pancreatic enucleation is associated with shorter operative time and less blood loss than occurs with formal pancreatic resection [3]. For patients with neuroendocrine tumors of the head or uncinate of the pancreas, the postoperative length of stay is significantly shorter (6.9 vs 9.3 days) for patients managed with enucleation compared with pancreaticoduodenectomy [4].

By preserving pancreatic parenchyma, enucleation of small pancreatic tumors is more likely to be associated with preservation of endocrine and exocrine function. Cauley and associates [3] have documented that both new endocrine and exocrine insufficiency are significantly less ($p < 0.05$) when enucleation is compared with resection. With a mean follow-up of approximately 4 years, they discovered new exocrine insufficiency in only 4% of patients after enucleation, and endocrine insufficiency in 2%. In comparison, both new exocrine and endocrine insufficiency were documented in 17% of patients undergoing resection [3].

In a series of small (<3 cm), low-risk neuroendocrine tumors without evidence of metastatic disease, Pitt et al. [4] have demonstrated an overall 5-year survival of 92%. In this analysis, there was no significant survival difference between the 36 patients treated with enucleation and the 86 treated with resection [4].

18.7 Conclusions

Pancreatic enucleation should be considered for relatively small, benign or premalignant lesions of the pancreas. Both short-term and long-term advantages of enucleation over resection have clearly been demonstrated for lesions not involving the main pancreatic duct. Compared with either pancreaticoduodenectomy or distal pancreatectomy, pancreatic enucleation allows for greater preservation of pancreatic function and is associated with lower mortality and equivalent long-term survival.

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Part VI

Other Neuroendocrine

Small Bowel Resection and Lymphadenectomy for Jejunoileal Neuroendocrine Tumors

19

James R. Howe

19.1 Introduction

The small bowel is one of the most common sites of origin of neuroendocrine tumors (NETs) in general, and small bowel neuroendocrine tumors (SBNETs) are the most common gastroenteropancreatic NETs. The incidence of SBNETs increased fourfold between 1973 and 2002, and has overtaken adenocarcinoma as the most common histology [1]. Whether this represents improved diagnosis, widespread use of proton pump inhibitors, or changing environmental influences is unknown.

Some patients, especially those with liver metastases, may manifest symptoms of carcinoid syndrome, which include flushing, diarrhea, wheezing, and right-sided heart disease. Others may present with symptoms of bowel obstruction or anemia, but many may be asymptomatic until they develop pain from liver metastases.

SBNET primaries are predominantly located in the ileum; they are multifocal in 25% of cases [2]. Of these, 29% are localized to the bowel at diagnosis, 41% have involved regional nodes, and 30% have metastatic disease. Nevertheless, the overall median survival is 88 months: 111 months for those with localized tumors, 105 months with regional involvement, and 56 months for patients with metastatic disease [3]. Because of this generally favorable prognosis, an aggressive approach of resecting the primary tumor and regional lymph nodes is advised, with cytoreduction of liver metastases when possible.

One of the difficulties with SBNETs is the lack of a preoperative diagnosis. Many patients present with liver lesions, which upon biopsy reveal metastatic NET of unknown primary site. In this situation, one must suspect a gastroenteropancreatic site, with SBNETs and pancreatic NETs being the most common. Pancreatic NETs are usually visible on CT scan, but SBNETs may not be. One of the best clues pointing to an SBNET primary is the presence of mesenteric lymphadenopathy as one follows the segmental branches from the superior mesenteric artery (SMA) and superior mesenteric vein (SMV). Enlarged nodes in this region, which often contain calcifications, are the telltale sign of a small bowel primary.

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19.2 Operative Technique

19.2.1 Approach

Although laparoscopic surgery has gained popularity for treatment of colorectal neoplasms, its use should be strongly cautioned in SBNETs for several reasons:

- These tumors are frequently very small; palpation using the fingertips is important and cannot be substituted for by laparoscopic graspers.
- The lesions may be multiple, and additional small lesions may be missed even though larger primaries may be evident laparoscopically.
- The incision used for extracorporeal anastomosis is generally inadequate to perform extended regional node dissection, cholecystectomy, and concomitant liver cytoreduction.

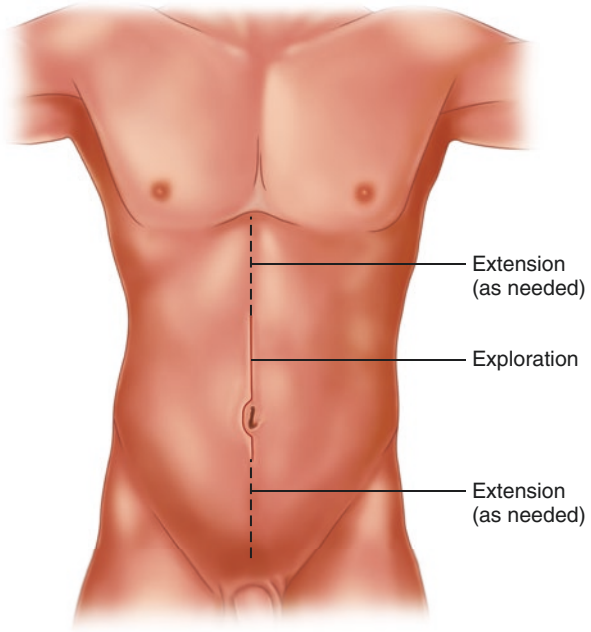
For these reasons, a midline incision is preferred. If preoperative imaging shows minimal nodal disease and no liver metastases, a smaller incision beginning just below the umbilicus and extending towards the epigastrium may be used for combined small bowel resection, regional lymphadenectomy, and cholecystectomy. When the nodal disease is more substantial and if the liver is involved, a generous midline incision from the xiphoid to between the pubis and umbilicus should be used (Fig. 19.1). During the operation, if the patient has liver metastases, we will infuse octreotide at a rate of 100 μg/h to help avoid intraoperative hypotension associated with the release of vasoactive hormones. Postoperatively, the drip is decreased to 75 μg/h, and then reduced by increments of 25 μg/h every 8 h.

J.R. Howe (ed.), *Endocrine and Neuroendocrine Surgery*, Springer Surgery Atlas Series, DOI 10.1007/978-3-662-54067-1_19

Figure 19.1

Incisions used for small bowel neuroendocrine tumor (SBNET) resection. If only the small bowel tumor, regional nodes, and gallbladder are to be resected, then a 5- to 6-inch midline incision may be used (*solid line*). If more extensive surgery is required, including extended nodal dissection, removal of peritoneal implants, or hepatic cytoreduction, then a long midline incision is preferred (*solid and dotted lines*)

Figure 19.1



19.2.2 Exploring the Abdomen

Once the peritoneal cavity is entered, a thorough exploration is carried out. This exploration begins with division of the falciform ligament, followed by careful bimanual palpation of both the right and left lobes of the liver. Liver metastases are very common, occurring in 30% of cases of SBNETs in the Surveillance, Epidemiology, and End Results (SEER) Program registries [3] and in 77% of our patients at a tertiary referral center [2]. Compare the intraoperative findings with the results of preoperative imaging, including CT scans and octreoscans, where available. Assess whether the liver disease, if present, consists of relatively few, large lesions, which may be amenable to debulking, or whether there are numerous, small lesions in both lobes, where it will be difficult to make a substantive impact on reducing the tumor burden. Also assess whether many of the lesions are peripheral and subcapsular (and therefore amenable to enucleation) or deep, requiring formal resection or ablation.

Next, palpate the gallbladder for stones, palpate the hepatoduodenal ligament for enlarged nodes, and assess for aberrant hepatic arterial anatomy. Palpate the stomach and then the duodenum for any intramural or serosal nodules. Feel the peritoneal surfaces under each diaphragm for nodularity, and then run a hand down along the anterior peritoneum and lateral peritoneal surfaces, and then to the pelvis. Feel for the catheter balloon in the bladder, and then follow the sigmoid down for lesions known as drop metastases. When the peritoneal reflection is reached, feel anteriorly for the uterus and then each ovary in female patients. Enlarged, hard ovaries are likely to represent metastases and should be removed, especially in postmenopausal women. Follow the sigmoid colon with your hand up to the splenic flexure, palpating for lesions, then across the transverse colon, then down the ascending colon to the appendix.

Locate the ligament of Treitz; then pull the jejunum upward and carefully inspect and palpate the entire small bowel to the ileocecal valve, grasping the bowel between thumb and

Figure 19.2

Palpation of the small bowel. Beginning at the ligament of Treitz, carefully pull the small bowel through thumb and forefinger to assess for lesions. Mark each lesion with a stitch, or mark the first and last lesions, if they are multiple

forefinger and methodically pulling the bowel through these fingers, palpating for intramural lesions (Fig. 19.2). Lesions as small as 1–2 mm can be detected, but most tumors will be between 5 and 15 mm in size. Pull 10–15 cm of bowel through the fingers of the left hand while firmly grasping the starting point with the right hand; then re-grasp the bowel distally with the right hand adjacent to the left, and pull the next 10–15 cm through; repeat until the ileocecal valve is encountered, which is generally 300–600 cm from the ligament of Treitz. Most lesions will be in the distal jejunum to the terminal ileum; it is rare to find lesions in the proximal part of the jejunum. Multiple lesions are found in 30–40% of patients; if several lesions are encountered, place a 3-0 silk suture in the serosa of the bowel adjacent to each one. If there are many lesions (the most I have found is 139), then place a suture just proximal and distal to the first and last ones. We measure and record the total length of the small bowel and the segment of bowel affected by both the tumor(s) and lymphadenopathy, which helps in planning the resection.

Palpate the mesentery supplying the bowel adjacent to the lesions you have found, to locate grossly enlarged nodes (Fig. 19.3). Assess their size and compare them with the preoperative CT scan, which commonly shows enlarged nodes with calcification in the small bowel mesentery. Carefully follow the mesenteric vessels on the CT scan and look for enlarged nodes proximally, which can extend up to the lower border of the pancreas and may encircle the SMV and SMA. Now assess the mesentery for the most proximal extent of enlarged or firm nodes, and note their relationship to major vascular branches (such as the ileocolic) versus more central and critical vessels such as the SMV and SMA. The nodes may be matted down and pulling loops of bowel into them, as well as being heavily calcified and thick. Determine the relationship between these nodes and the lesion(s) within the bowel, and how these will be removed together. If multiple loops of bowel are adherent to the nodes in the mesentery, it may be necessary to sharply dissect them off these nodes so that the extent of nodal involvement can be better appreciated.

Figure 19.2

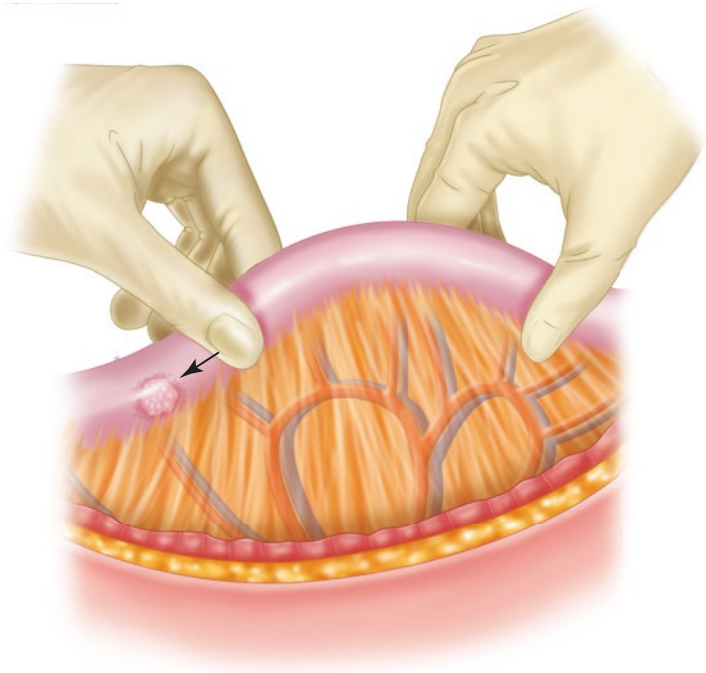
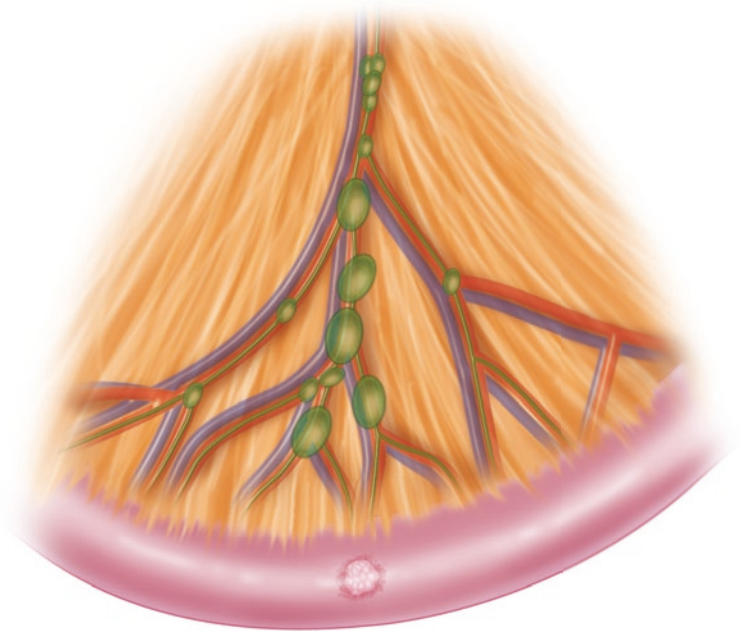


Figure 19.3

Distribution of enlarged nodes in the small bowel mesentery.

Figure 19.3



19.2.3 Small Bowel Resection and Lymphadenectomy

The extent of resection depends upon the number of lesions, the location of the lesions, and the extent of lymphadenopathy. Single lesions in the jejunum or proximal ileum require a segmental bowel resection and regional lymphadenectomy, to encompass those nodes draining along the segmental vessels supplying that portion of the small bowel (Fig. 19.4). If there is a single lesion without bulky central mesenteric lymphadenopathy, resection of approximately 30 cm of small bowel is generally required.

If there are multiple lesions, one must carefully consider how much bowel should be resected. It is generally preferable to remove one long segment and have one anastomosis, rather than removing multiple segments and having two or more anastomoses. If multiple resections and anastomoses are planned and an adequate lymphadenectomy is performed, one needs to take into account whether the blood supply to the intervening bowel segment may be compromised. Prior to resection, measure the length of bowel from the ligament of Treitz to the proposed site of transection, then from the distal resection margin to the ileocecal valve; carefully record these numbers. Also measure the length of bowel within the proposed lines of transection. Most patients will have 300–600 cm of small bowel, and even with multifocal tumor or significant involvement of the mesentery, we try to keep resections to less than 100 cm. Short-gut syndrome is a risk if one cannot preserve about 200 cm of bowel. Preservation of the ileocecal valve, if possible, can help the situation. If there are very small lesions distant from the main tumor(s), for which lymph node involvement would be unlikely (such as with lesions smaller than 2–4 mm), one might consider local excision of these lesions in order to preserve more bowel length.

Many lesions are found right at the ileocecal valve or in the terminal 30 cm of the ileum. To perform an adequate lymphadenectomy, the ileocolic artery and vein must be sacrificed (Fig. 19.4), so the terminal 20–30 cm of ileum, as well as the right colon, will be devascularized and must be removed. How much colon to remove will depend on the adequacy of flow from either the middle colic or right colic artery to the hepatic flexure. If a good pulse can be palpated in the adjacent mesentery, I try to save the hepatic flexure and perform an anastomosis of the proximal small bowel to the colon just below the right colic artery in the upper ascending colon.

Once the transection points of the bowel have been determined, create a small opening in the mesentery adjacent to the small bowel using electrocautery or a clamp. Place a GIA™-80 stapler (Medtronic–Covidien; Minneapolis, MN, USA) through this, then transect the bowel using a blue (3.5-mm) load. Repeat this procedure for the distal site of the transection in the colon or small bowel. Next, score the mesentery leading away from the point of transection, converging with a similar line from the other point of transection, carefully including the major segmental vessels and their lymph nodes.

Figure 19.4

Path of lymphatic drainage from (1) terminal ileal NET, and (2) jejunal or proximal ileal NET. *Dotted lines* designate the lines of transection of the bowel and mesentery. *Arrows* show the direction of nodal spread from the small bowel wall along segmental blood vessels to the root of the superior mesenteric artery (SMA)

Make sure to include all these nodes and any others that appear enlarged. Divide the mesentery between clamps, then suture ligate with 2-0 silk sutures, or alternatively, use a device such as the LigaSure™ Impact (Medtronic–Covidien). Continue this dissection until the point where the segmental vessel comes off the SMA. There will often be nodes at this point, which can be carefully dissected from the base of this vessel by dividing the soft tissue over the surface of the vessel. I recommend holding the nodes and segmental vessel in one hand and pulling them away from the SMA; then take small amounts of the fibrofatty tissue at a time with electrocautery or the LigaSure™. Rotate the nodes while palpating the vessel to finish dividing the tissue, until the takeoff of the artery and vein from the SMA and SMV is directly visualized. Pull the nodes toward the specimen, freeing up the area 1 cm from the surface of the SMA and SMV; then doubly clamp the artery and vein (Fig. 19.5). Divide between the clamps and pass off the specimen. Suture ligate the segmental vessels with 2-0 silk without encroaching upon the main trunk of the SMA and SMV. When hemostasis has been achieved, assess the color of the bowel at the transection sites, and try to palpate a pulse in the subsegmental artery feeding each side. Sometimes an additional 5–10 cm of small bowel (usually proximally) should be resected if it has a congested appearance and there may be questions regarding inflow. As long as there is adequate length of bowel, one should have a low threshold to resect such segments.

Once viability of the two ends of the bowel has been confirmed, it is time to perform the anastomosis. The anastomosis is performed by suturing the mesenteric edges of the two ends of the bowel limbs approximately 2 and 8 cm from the staple line using 3-0 silk sutures. Place atraumatic bowel clamps 10 cm proximally and distally to minimize spillage. Next, cut off the antimesenteric 1-cm edge of the staple line on both limbs of bowel and insert each half of a GIA™-80 blue load stapler into the lumen (Fig. 19.6). Clamp each half of the stapler together, ensuring that the mesentery is not between them, and then fire the stapler load. Remove the stapler, holding the bowel vertically with Allis clamps to avoid leakage of intestinal contents, then approximate the two sides of the enterotomy with additional Allis clamps, making sure that the GIA™ staple lines are offset from one another. Fire a TA™-60 stapler (Medtronic–Covidien) blue load (3.5 mm) under the Allis clamps to close the enterotomy. Oversewing the staple line with a running 3-0 PDS inverting suture is optional at this point. Reapproximate the edges of both sides of the mesentery using a running 3-0 Vicryl suture to obviate internal hernia and aid with hemostasis (Fig. 19.7).

At the end of resection and lymphadenectomy, it is important to carefully assess the remaining bowel. If either end appears to have compromised inflow or venous outflow, resect additional bowel at that time. It is usually better to ensure well-perfused bowel and risk some shortened length than to have a leak from the anastomosis.

Figure 19.4

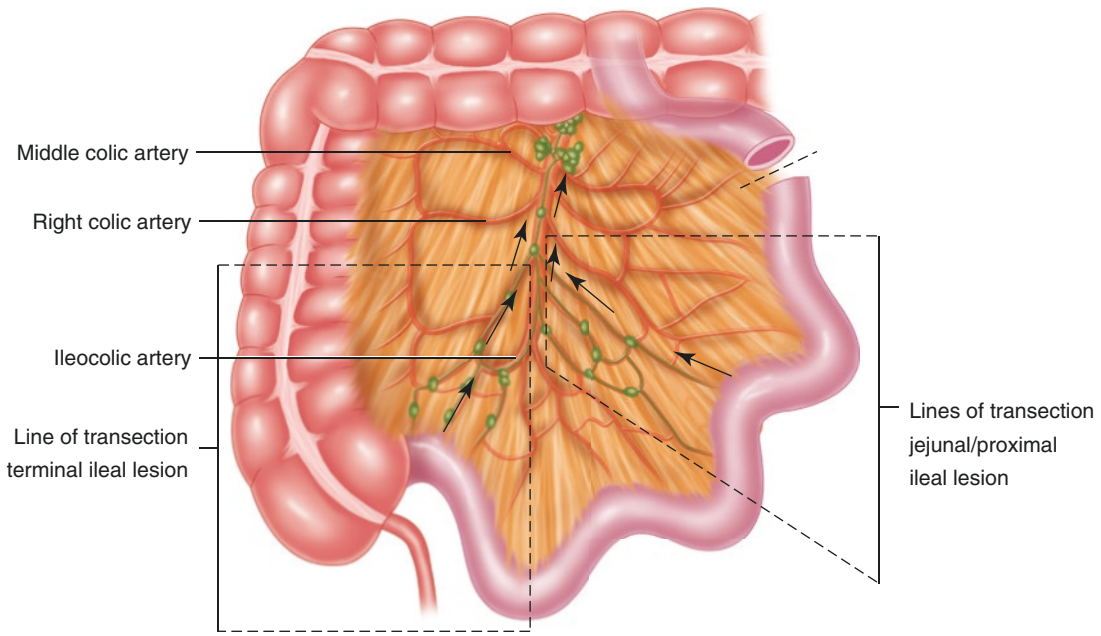


Figure 19.5

Circumferential dissection of the base of the ileocolic artery, pulling the nodes down away from the SMA and superior mesenteric vein (SMV). Once the base of the mesentery is freed of nodes (*dashed line*), doubly clamp and suture ligate the proximal subsegmental vessels

Figure 19.6

(**a**) Placement of the GIA™-80 stapler through the cut ends of the bowel at the antimesenteric side. (**b**) Closure of the enterostomy with a TA™-60 stapler

Figure 19.5

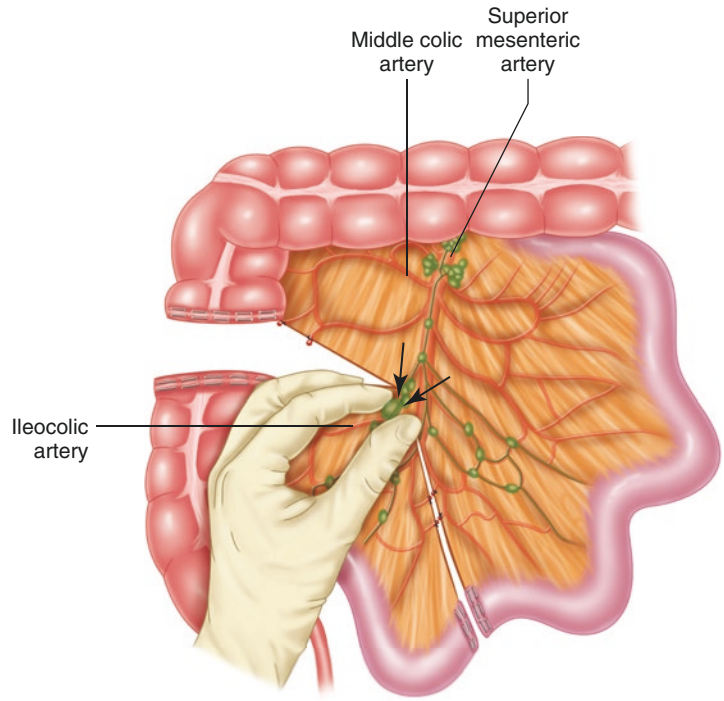


Figure 19.6

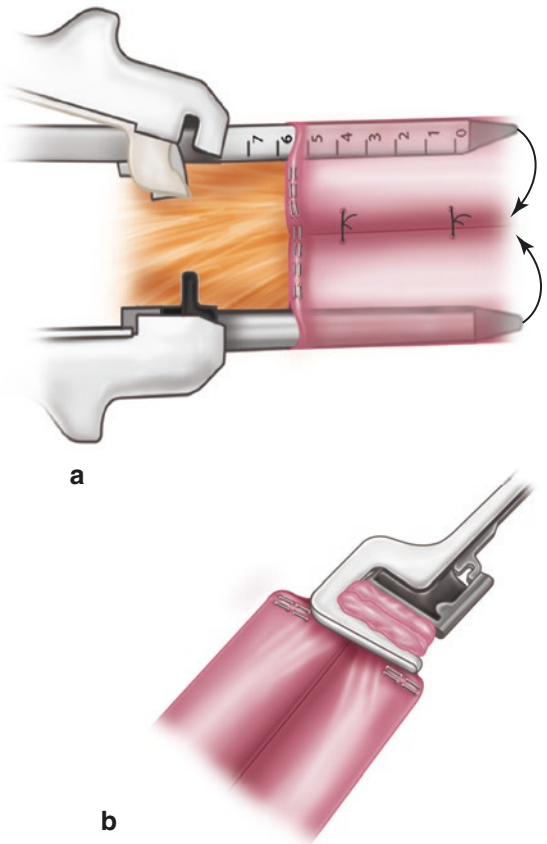
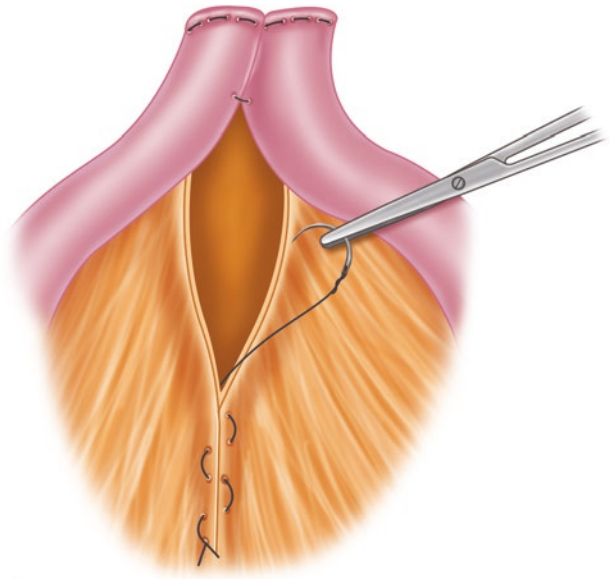


Figure 19.7

Closure of the peritoneum overlying the cut edges of the mesentery

Figure 19.7



19.2.4 Special Considerations for Lymphadenectomy

It is not uncommon for nodes to continue above the takeoff of the segmental vessels from the SMA and SMV, either as individual, enlarged nodes or a mass at the mesenteric root. Individual nodes can be removed by opening the peritoneum of the mesentery and carefully dissecting each one out circumferentially. It is important in this process not to injure the SMA or SMV, so as not to compromise inflow or outflow to the remaining bowel. On the other hand, a nodal mass extending to the root of the mesentery is often hard and flat, and encases the mesenteric vessels. In this circumstance, it is very difficult and often inadvisable to persist with the lymphadenectomy because of the risk of mesenteric vascular injury. An exception is when there are large, discrete nodes with clear boundaries rather than the more common hard, calcific mass. Leaving this kind of proximal mesenteric mass is recommended, as patients can still have extended survival, and these lesions can often remain stable in size over years. Some patients have mesenteric root masses in the absence of liver metastases, and may not develop metastases for several years.

One argument for attempted resection of a mesenteric root mass is venous insufficiency and abdominal pain, but it has been my experience that most patients develop collateral venous drainage and do not have significant abdominal pain. Some of these patients do have thickened loops of small bowel, but these are resected with the primary tumor and are the most likely affected portions of the bowel. Some surgeons have advocated splitting the nodal mass down to the mesenteric vessels, and then peeling the mass off the vessels. This is a very technically challenging endeavor, as these masses are often heavily calcified, making it very difficult to know where the vessels are. Attempting to divide the nodal mass without entering the mesenteric vessels risks significant blood loss and possible vascular compromise to the remaining bowel.

Some patients will have yet another, higher group of nodes along the mesenteric root, just below or behind the inferior margin of the pancreas. These nodes are hard to access, requiring an approach through the lesser sac. The risks of tackling these nodes are similar to the risks of tackling the nodes at the mesenteric root below the mesocolon, namely the hazard of injury to the mesenteric vessels. If the nodes are round and discrete, they may be peeled off, but beware of a flat, dense, calcified group of congruent nodes. Small bowel lesions also are occasionally accompanied by large aortocaval masses, portocaval, pararenal, or even celiac nodal lesions. Sometimes these are calcified, and preoperative CT scans or endoscopic ultrasound may even mistakenly identify them as primary pancreatic tumors. In reality, these masses represent more proximal extension of SBNET nodal disease. That is why it is very important to run the bowel and look for a small bowel tumor even when a pancreaticoduodenectomy is planned for what appears to be a primary pancreatic NET. The finding of a small bowel lesion with mesenteric lymphadenopathy at this point should make one hesitate to continue with that procedure but instead perform a small bowel resection with mesenteric lymphadenectomy, with possible extension to these peripancreatic nodes. Although these nodes may be large and adherent to nearby vascular structures, they may be freed up and removed by careful dissection. If the nodes extend into the aortocaval area near the pancreas, the nodes posterior to the portal vein should be evaluated, as they also may be involved. During these extended nodal dissections, one must keep in mind the generally favorable survival of patients with SBNETs, and weigh this against the potential risk of removing these nodes.

19.2.5 Other Considerations

Patients whose tumors have grown through the serosa of the bowel are at risk for peritoneal seeding. This seeding may manifest as plaques of tumor along the diaphragm, mesentery, small bowel, colon, and pelvic structures. Such lesions should be removed if possible, but sometimes there are so many areas that doing so becomes unrealistic. Small plaques can be treated with the argon beam coagulator to avoid the need for resection. Bulkier deposits may require omentectomy, small bowel resection, or even sigmoid resection. Again, it is important to weigh the risks and benefits of resecting bowel, but these patients will often live for many years, so areas of impending obstruction should be treated. In these cases, it is important to check for ovarian involvement, which is common.

Many patients with SBNETs (especially those with nodal and/or liver involvement) will end up receiving long-term treatment with somatostatin analogues. Over time, this will lead to cholelithiasis, and the potential for future biliary colic or acute cholecystitis. Patients undergoing embolization for unresectable liver metastases are at risk for gallbladder necrosis. For these reasons, a cholecystectomy should generally be performed at the initial operation for SBNETs, unless it is an early stage tumor.

More than 30% of patients with SBNETs will have synchronous liver metastases, and debulking of these lesions can lead to improved long-term survival. Therefore, it has been our practice to remove the SBNET primary lesion and accompanying nodal disease, then move on to cholecystectomy and debulking of liver lesions. Because of the very high recurrence rate, we favor hepatic parenchymal preservation through enucleation and targeted ablation (which usually can be accomplished through the same midline incision used for bowel resection and lymphadenectomy) rather than extended hepatic resections.

19.3 Complications

Patients do surprisingly well after these procedures, depending upon the extent of disease. Diarrhea is the most common complication of bowel resection, especially resection of the terminal ileum or greater lengths of bowel. This diarrhea can be due to malabsorption secondary to short bowel (treated with loperamide), failure of reabsorption of bile salts in the ileum (treated with cholestyramine), or fat malabsorption caused by inhibition of pancreatic enzyme secretion mediated by somatostatin analogues (treated with pancreatic enzymes).

When the involved nodes extend proximally to involve the root of the mesentery, some patients will develop mesenteric venous obstruction, which may be seen on CT scans as thickened loops of small bowel with numerous collaterals. Patients may have symptoms of abdominal pain (which may be worse after eating), but some are relatively asymptomatic. If collaterals have developed, little intervention may be needed, but when symptoms develop, one should consider either anticoagulation or resection of the involved segment of bowel. If the nodal disease is resectable, resection would be another option, but this is rarely the case.

19.4 Results

Patients with SBNETs benefit from resection of the primary, even in the presence of metastatic disease. In a retrospective review, Hellman et al. [4] looked at patients with midgut carcinoids and found a median survival of 7.4 years in those undergoing resection of their primary (n = 249) versus 4.0 years for patients with no resection or palliative procedures (n = 63; $P < 0.01$). They also found that for patients with their primaries removed, resection of involved nodes (n = 166) versus leaving them behind (n = 83) led to improved median survival of 7.9 versus 6.2 years ($P < 0.001$). Of course, there was a high potential for selection bias inherent in this study. Givi et al. [5] reviewed 84 patients with unresectable liver metastases; 60 had their primaries removed and 24 did not. They found 81% 5-year survival in those with resection of the primary tumor versus 21% in those without resection ($P < 0.001$). They believed that there was not significant selection bias in their study, and that the improved survival was due to reduced progression within the liver metastases. An international collaborative study examined patients from eight centers who had liver-directed surgeries for metastatic NETs from various sites, and found 74% 5-year survival, versus 54% in the most recent SEER data, suggesting that hepatic debulking does improve survival [6]. Most patients will develop recurrent hepatic disease, however; it occurred in 84% of patients at 5 years in the series of Sarmiento et al. [7]. Overall 5-year survival reported for patients in the SEER database is 65% for those with localized disease, 71% for those with regional disease, and 54% for those with metastatic disease [3].

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Liver Surgery for Neuroendocrine Tumors

20

J. Philip Boudreaux and Yi-Zarn Wang

20.1 Introduction

Neuroendocrine tumors (NETs) comprise approximately 10% of metastatic liver lesions. Formal hepatic lobectomy is rarely indicated because approximately 80–90% of metastases are multifocal and bilateral. The most frequent cause of death in patients with metastatic NETs is liver failure resulting from hepatic replacement by tumor [1, 2]. Five-year survival in patients with liver metastases has been reported at 30–50%, but 5- and 10-year survival rates greater than 80% can be achieved with aggressive surgical and multimodal therapy [3]. The goals of therapy should be prolongation of survival, objective tumor control, symptom control and biochemical control of functional tumors, and improvement in quality of life. Hepatic cytoreductive surgery performed for a curative or palliative intent can provide long-lasting benefit.

Because most metastases are bilateral, formal hepatic lobectomies are rare. To preserve the maximum amount of normal hepatic tissue, multiple segmentectomies or subsegmentectomies are more commonly performed. Nonanatomical metastectomies, enucleation, radiofrequency or microwave ablation, and irreversible electroporation are also used to cytoreduce tumor burden, either singly or in combination. Selectively, liver transplantation may be an option if extrahepatic disease can be controlled or eliminated. Multivisceral transplants (en bloc liver, stomach, intestine, and pancreas) are now being performed for metastatic disease at the mesenteric root with liver and pancreatic metastases.

The choice of specific technique and its timing should be ascertained by a multidisciplinary consensus when evaluating the patient with liver metastases [2, 4]. Every effort should be made to resect the primary tumor initially or at the time of liver resection. A certain percentage of patients with "unknown primaries" will have their primary discovered at the time of liver resection. Simultaneous resection of the primary tumor should be performed in healthy patients. In patients with advanced disease who have intestinal obstruction and/or ischemia and malnutrition, the intestinal obstruction and intestinal ischemia should be addressed first. After nutritional rescue, the patient may then safely undergo major hepatic cytoreduction [2].

Selection criteria for surgical resection should include having less than 50% of the liver parenchyma involved with tumor. The presence of tumor abutting or encircling vascular or biliary structures is not an absolute contraindication to surgery. Many times the tumors will displace these structures without invasion. When major vascular or biliary structures are encased, we have successfully used irreversible electroporation (IRE) to avoid collateral damage from the heat generation that occurs with radiofrequency ablation or microwave energy. Radiofrequency ablation, microwave ablation, or IRE is best reserved for tumors 3 cm or less in diameter [3].

Preoperative preparation is critical to successful hepatic surgery in patients with functional NETs. A relative contraindication to liver resection is the presence of right-sided heart failure, a condition more likely to occur in patients with carcinoid syndrome and elevated 5-hydroxyindoleacetic acid (5HIAA) levels. In addition to addressing malnutrition and fluid and electrolyte losses from the gastrointestinal tract, attention must be given to the prevention of carcinoid crisis intraoperatively. Manipulation of a functional serotonin-producing tumor can lead to cardiovascular collapse unless somatostatin analogue blockade is initiated preoperatively. We recommend an intravenous bolus of octreotide (250–500 μg) followed by a continuous infusion of 250–500 μg per hour. Using this protocol, we have limited the incidence of carcinoid-induced hypotension to less than 3% in our last 220 liver resections [5]. Volume expansion, antihistamines, H2 blockers, and steroids serve as adjuncts to block the serotonin response intraoperatively, and they can also reduce carcinoid-induced asthma [2]. We recommend avoiding vasopressors such as epinephrine, which can precipitate massive serotonin release and irreversible carcinoid crisis. We have successfully used low-dose dopamine, vasopressin, and

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J.R. Howe (ed.), *Endocrine and Neuroendocrine Surgery*, Springer Surgery Atlas Series, DOI 10.1007/978-3-662-54067-1_20

phenylephrine hydrochloride (Neo-Synephrine) when pressor support was required after the initiation of high-dose octreotide therapy.

In cases of bilobar disease, there usually will be several dominant, large lesions and several smaller lesions. In an effort to achieve at least a 70–90% debulking, the larger lesions can be individually excised and the smaller lesions (usually less than 3 cm) can be treated with radiofrequency ablation or IRE. In the case of a diminutive left lobe, a staged procedure is used. The left lobe can be debulked initially and the right portal vein embolized, causing some regression of the right hepatic lobe and hemihypertrophy of the left, followed by resection of the right hepatic lobe 6 weeks after embolization [4].

20.2 Radiofrequency Ablation and Microwave Ablation

Although the wavelength energies are different, we will consider radiofrequency ablation (RFA) and microwave ablation together. Both rely on high-frequency (radio wavelength) alternating current to generate heat in excess of 100 °C in a defined space dictated by the "antenna" probe placed directly into the tumor. We use this technology when faced with small tumors (3 cm or less) deep within the hepatic parenchyma, to spare normal hepatic tissue that would otherwise be lost by a large resection. We use this method when the tumors are not near hilar structures, in order to avoid collateral heat injury to those areas.

The RFA needle is typically placed under ultrasound guidance, and the tines are deployed to the desired length depending upon lesion size and desired margin (Figs. 20.1 and 20.2). After ablation, we retract the tines, rotate the probe 45°, redeploy, and repeat the ablation to increase cell killing in all fields defined by the probe. Track ablation is used as the needle is withdrawn to achieve hemostasis and decrease the risk of seeding along the needle track.

Microwave ablation uses a different probe with a slightly larger diameter (14 gauge *vs* 18 gauge) with a single straight needle; no tines are deployed. The size of the ablation is directly related to the length of time the device is energized and the power setting. A longer ablation time means a larger zone of ablation. Some manufacturers also provide for ablation of the track as the needle is removed.

The main limitations of both technologies are size and location of tumors near vital structures within the liver. It is difficult to achieve complete killing in tumors larger than 3 cm, and when ablations are performed near larger blood vessels, a heat sink phenomenon can occur. The rapid flow of blood near an ablation site will cool the tissue to sublethal temperatures, and incomplete killing may occur. The phenomenon occurs more commonly with RFA, while microwave tends to continue to heat (and potentially injure or destroy) these blood vessels and associated bile ducts. One can at least partially prevent this heat sink effect by using the Pringle maneuver during ablation to obtain more even heat distribution. We usually pretreat the patient with mannitol and induce a brisk diuresis prior to ablation to minimize renal injury from tumor lysis syndrome. If multiple ablations are performed, the patient's core temperature may rise considerably and the heating blanket must be turned off. Postablation scanning usually displays avascular lesions remaining within the liver (Fig. 20.3).

Figure 20.1

Radiofrequency ablation (RFA). (**a**) Probe being advanced into the lesion, usually under ultrasound guidance. (**b**) Deploying the tines to the just beyond the edges of the lesion. (**c**) Zone of ablation extending beyond the tumor

20.3 Irreversible Electroporation

Irreversible electroporation (IRE) is a new technology that uses very high voltage (1500 V/m^2) at very low direct current (nanoamperes) passing through tissue between the positive and negative electrodes for multiple brief pulses (nanoseconds). The flow of electricity creates irreparable holes in cell membranes, inducing apoptosis. This technique does not produce heat or destroy stromal framework, so it is desirable for use near intrahepatic blood vessels and bile ducts, where significant heat generation would produce collateral damage. Normal bile duct and endothelial cells repopulate along the remaining stromal framework. We employ IRE (NanoKnife®, AngioDynamics, Latham, NY, USA) when RFA would be too close to hilar structures to avoid damage to main bile ducts, usually for tumors of 3 cm or less. Two to four electrodes are placed into or near the tumor to create an electric current field of sufficient size to ablate the tumor (Fig. 20.4a).

Ultrasound or CT guidance is used to place the 18-gauge needles (Fig. 20.4b). It is important to place the electrodes parallel to each other in multiple planes to produce the desired current flow and maintain uniform tissue impedance. Placing needles 2.5 cm apart appears to be optimum spacing (Fig. 20.4c). It is also important to place the electrodes parallel to major vascular structures so as not to traverse the lumens with the needles, which will increase the risk of post-procedure thrombosis.

20.4 Tumor Enucleation

Often midgut NETs metastatic to the liver are surrounded by a pseudocapsule, and these tumors are very dense. They can be enucleated (Figs. 20.5 and 20.6) by crushing the hepatic parenchyma near the tumor with a hemostat, clipping the feeding structures with fine hemoclips, and tying the larger vessels prior to division. Alternatively, an energy resective device such as the LigaSure™ (Medtronic–Covidien, Minneapolis, MA, USA) can be used. Enucleation preserves the greatest amount of normal intervening liver and is useful for multiple or single superficial tumors of the liver. It also can be done laparoscopically. Despite positive margins of resection, recurrence rates remain low using this technique.

20.5 Segmental and Lobar Resections

More formal segmental or lobar resections are performed along the Couinaud resection lines (Fig. 20.7a) following the venous system. Ultrasound is used to note the location of the veins within the liver. The larger trunks are not amenable to sealing and dividing with the energy devices currently available (LigaSure™; Harmonic® scalpel, Ethicon Endo-Surgery, Cincinnati, OH; Aquamantys®, Medtronic, Minneapolis, MN), but the smaller branches entering the segments can usually be adequately sealed with these devices. The crush and clip or tie technique and/or an energy device is used to divide the hepatic parenchyma. Liver compression sutures of 2-0 chromic on a blunt needle are used as an adjunct for hemostasis along resection lines (Fig. 20.7b). Intraoperative ultrasound should be employed to map out the larger vascular structures; these can be divided with the endoscopic vascular stapler inserted directly into the hepatic parenchyma (Fig. 20.7c), or by conventional suture ligature. This technique is best applied to superficial lesions. Despite tumor cells at the margin, recurrence rates are generally low.

Figure 20.1

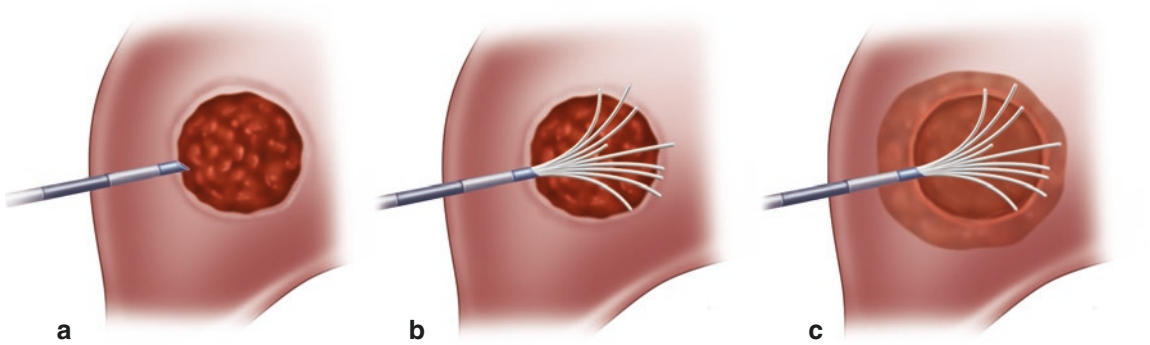


Figure 20.2

Image obtained under ultrasound during radiofrequency ablation. Note the needle advanced into the tumor in the posterior portion of the liver, with the white portion being the area within the tumor that has reached >100 °C

Figure 20.3

CT images of necrotic avascular tumors after RFA

Figure 20.2

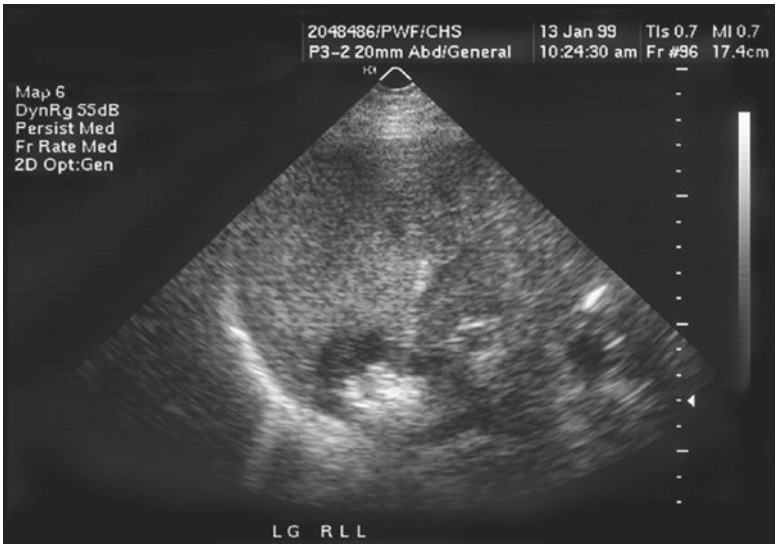


Figure 20.3

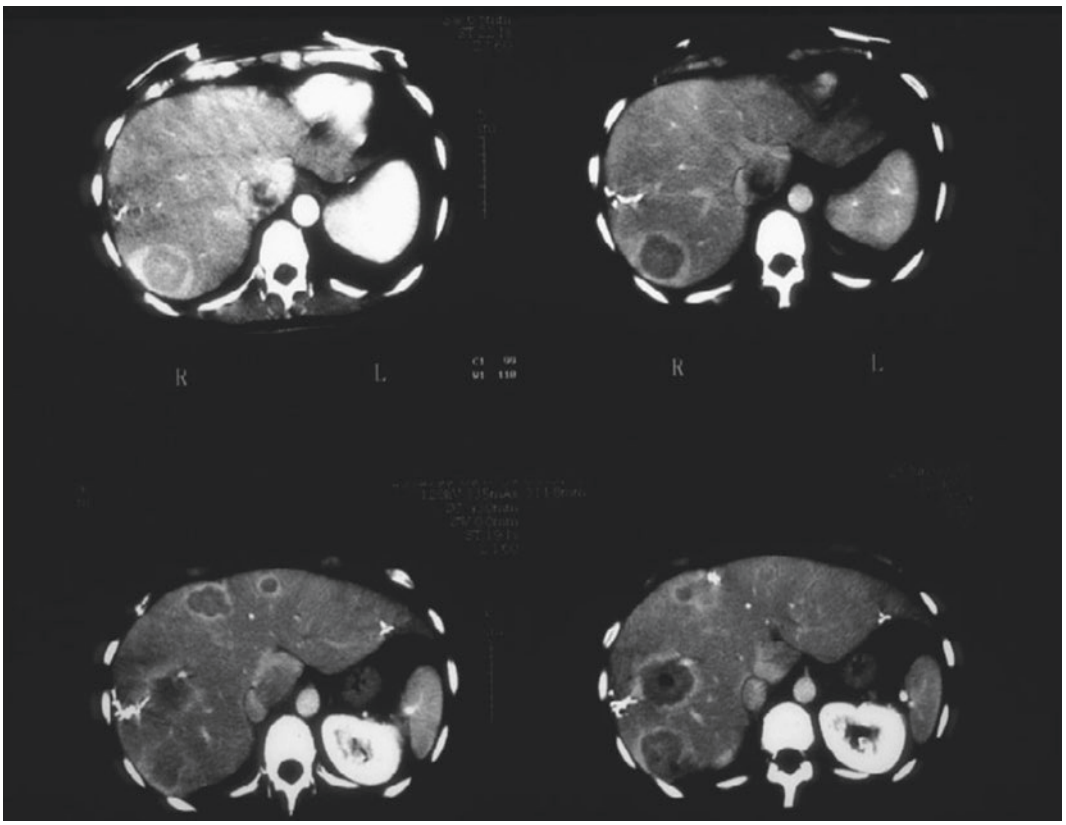


Figure 20.4

(**a**) Irreversible electroporation (IRE) electric field generated around the tumor. (**b**) Initial needle placement seen on CT scan for percutaneous technique. (**c**) Needle spacing

Figure 20.5

Neuroendocrine tumor (NET) after enucleation

Figure 20.4

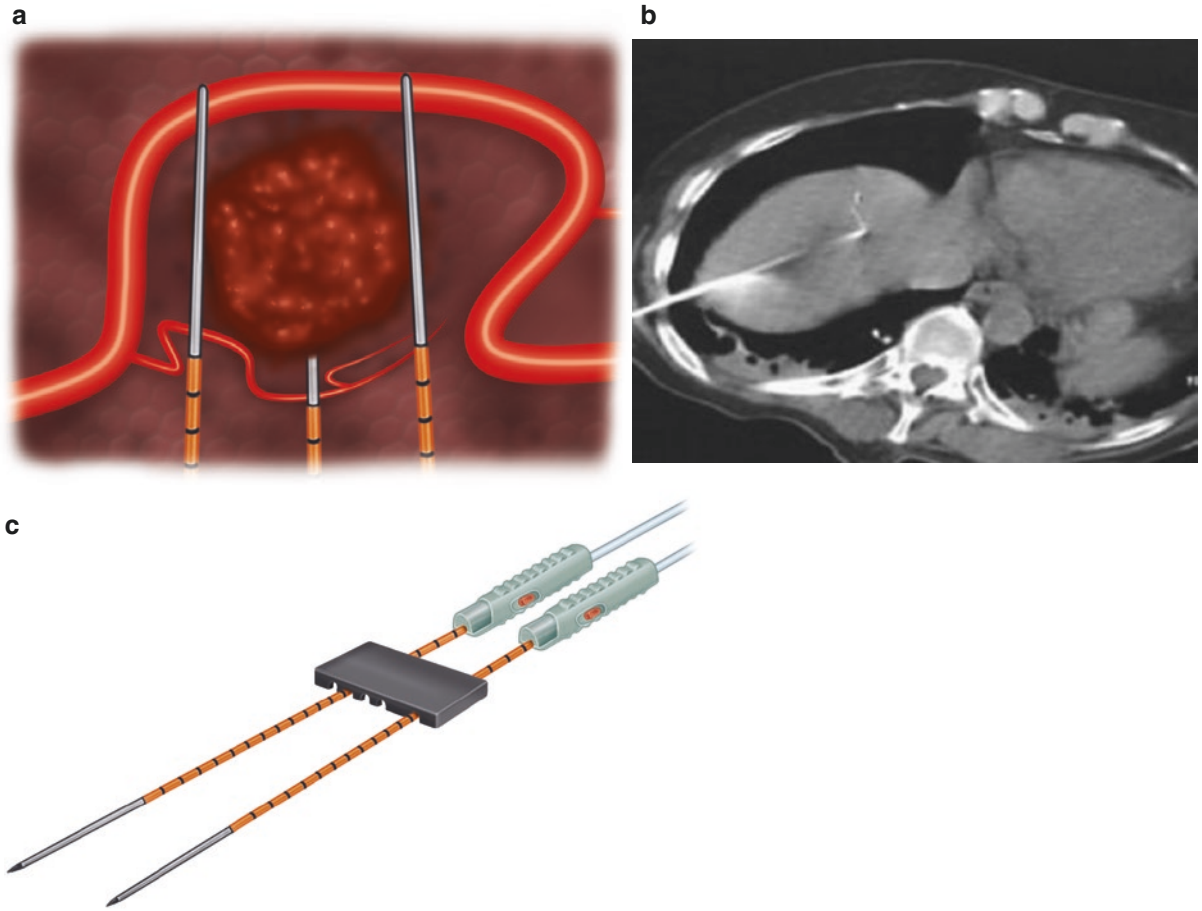


Figure 20.5

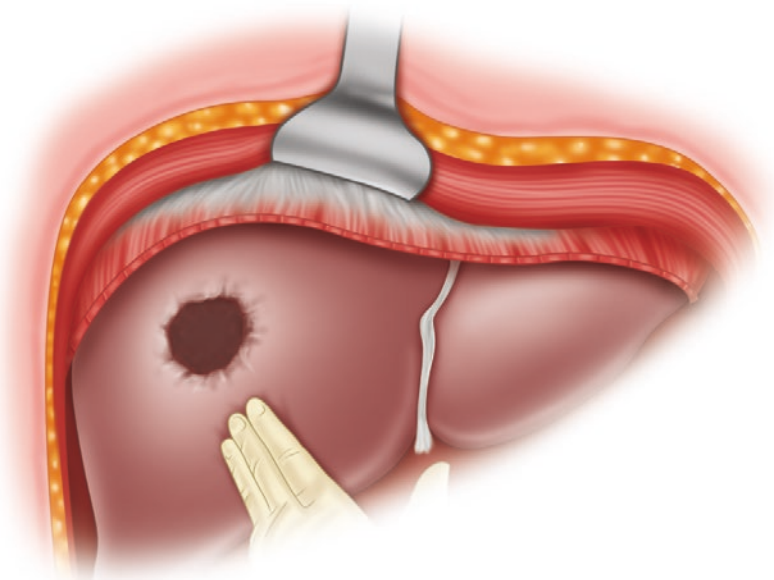


Figure 20.6

Enucleated NET specimen

Figure 20.7

(**a**) The Couinaud segmentation of the liver. (b) Liver compression sutures and parenchymal division with an energy device. (**c**) Use of an endovascular stapler in a left lateral segmentectomy

Figure 20.6

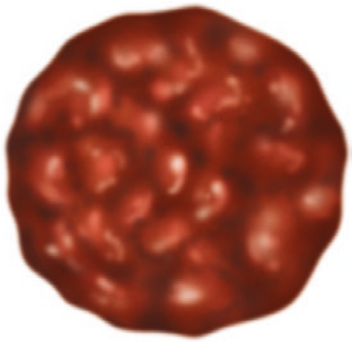


Figure 20.7

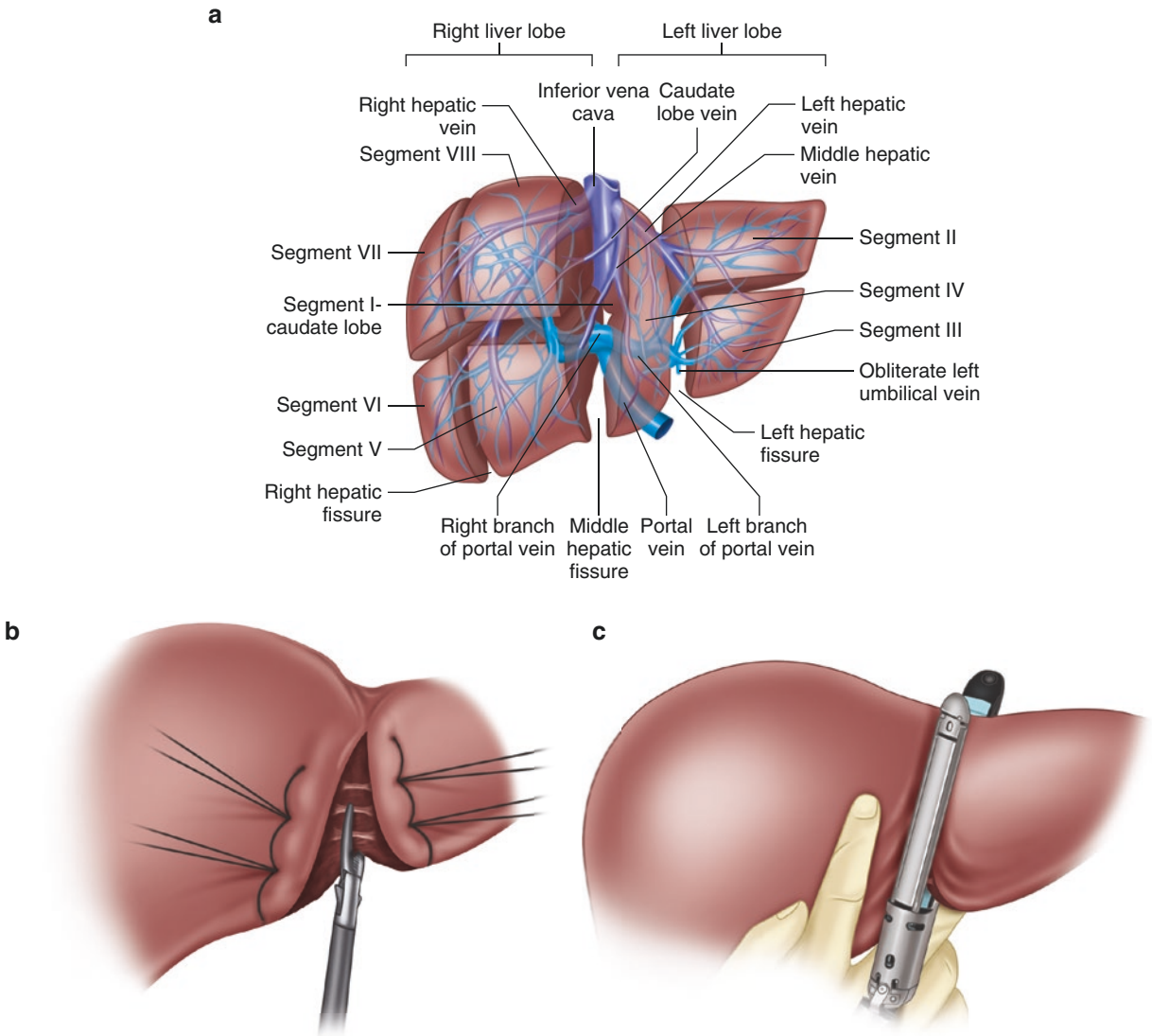
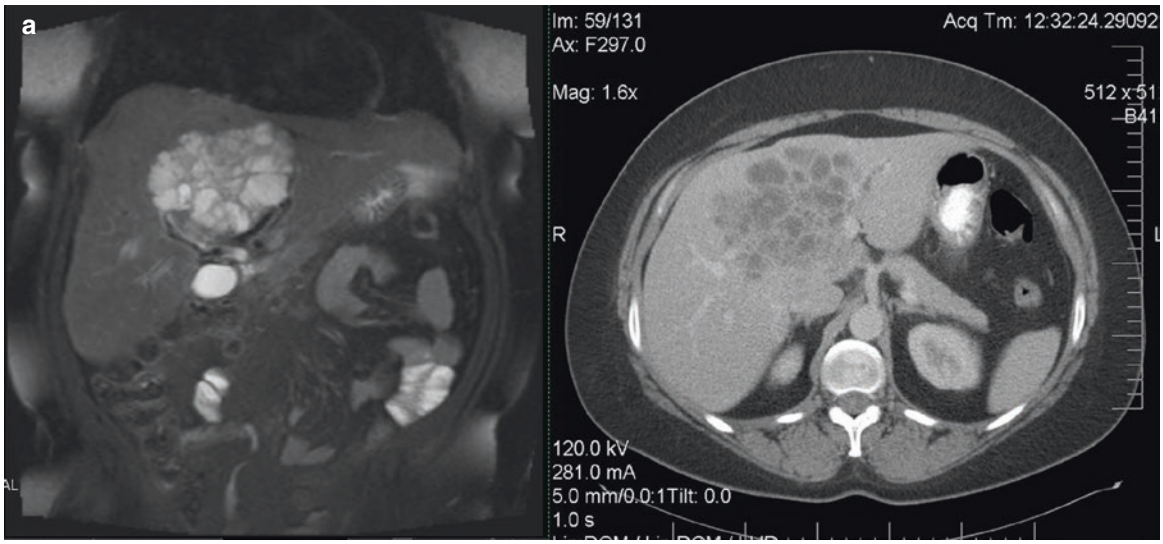
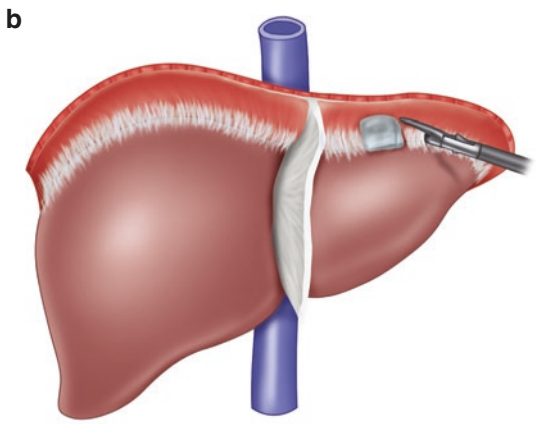


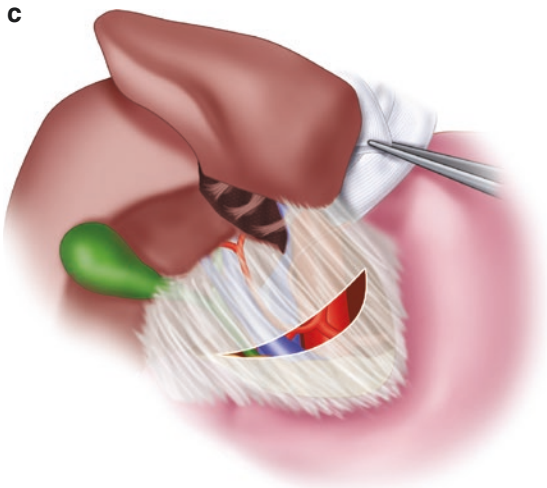
Figure 20.8

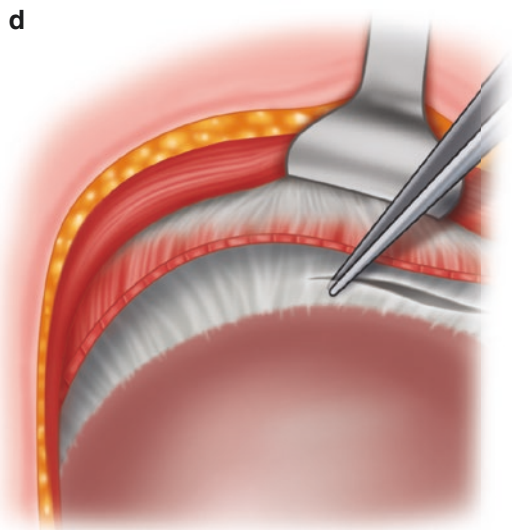
(**a**) A large central lesion splaying the portal veins, hepatic arteries, and biliary tree, as well as the left and right hepatic veins, in a patient with carcinoid syndrome. (**b**) Left lateral segment mobilization; the suprahepatic inferior vena cava (IVC) is to the left. (**c**) Division of the gastrohepatic ligament to expose the left side of the retrohepatic cava. The left lateral segment is rotated to the patient's right. (**d**) Right coronary ligament. Excessive traction prior to division will easily tear the liver capsule at this location

Figure 20.8


a
Im: 59/131
Ax: F297.0
Acq Tm: 12:32:24.29092
Mag: 1.6x
512 x 51
B41
R
120.0 kV
281.0 mA
5.0 mm/0.0:1Tilt: 0.0
1.0 s


b


c


d

20.6 Central Hepatectomy: Surgical Technique

Figure 20.8a shows a large central lesion splaying the portal veins, hepatic arteries, and biliary tree, as well as the left and right hepatic veins, in a patient with carcinoid syndrome. The middle hepatic vein is encased in tumor. To resect this tumor, the patient should be placed on high-dose octreotide infusion preoperatively. At operation, a 1-cm primary tumor was found in the terminal ileum and resected.

A key first step in all major hepatic resective surgery is to fully mobilize the liver for maximum exposure and ease of vascular control. All the ligamentous attachments of the liver are taken down. A laparotomy pad is placed behind the left lateral segment, and with downward traction on the liver, the ligament is divided with electrocautery, avoiding the left phrenic vein, with the pad protecting underlying structures (Fig. 20.8b). The gastrohepatic ligament is divided after rotating the lateral segment to the right (Fig. 20.8c). The coronary ligament and bare area of the liver are completely dissected off of the diaphragm by starting at the posterior inferior edge of the ligament (Fig. 20.8d). A Rumel tourniquet is placed around the porta hepatis for the subsequent Pringle maneuver. The hepatic veins are dissected and controlled (Fig. 20.9).

The anesthesiologist is instructed to maintain the central venous pressure at 0–4 mmHg and minimize crystalloid use during the resection. Urine output is maintained with mannitol infusion and albumin. The liver is mobilized off of the vena cava (Fig. 20.10).

The liver is scored with electrocautery circumferentially around the tumor, and dissection proceeds using crushing hemostats and hemoclips to divide the hepatic parenchyma immediately adjacent to the tumor. The dissection can be exceedingly difficult if the patient has had previous embolization therapy, because of the subsequent adhesions and neovascularity. The tumor is elevated off of the hilar structures and IRE is used to gain margins in this region without damage to the biliary or vascular structures. In a similar manner, adequate margins are obtained using IRE at the level of the hepatic veins with sacrifice of the middle vein. The Pringle maneuver is applied for 10 min with 5-min rest intervals for three applications during the deeper portions of the dissection as the tumor is excised from the liver substance and away from the hepatic and portal veins. After resection, additional hemostasis is achieved in the liver parenchyma using fibrin glue, direct pressure, and suture ligature when required (Fig. 20.11).

Figure 20.9

Dissection of the hepatic veins

20.7 Discussion

As have others, we have observed three major categories of metastatic disease of the liver:

- Type 1, a single metastasis of any size
- Type 2, isolated metastatic bulk accompanied by smaller deposits, always involving both lobes of the liver
- Type 3, disseminated metastatic spread with both liver lobes involved and little to no normal liver parenchyma

Most patients we see are of type 2. In addition, tumor biology is quite variable, ranging from indolent, slow-growing tumors with low mitotic index and low Ki-67 to poorly differentiated tumors with a high mitotic index and high Ki-67 score (mitotic index >20 mitoses per 10 high-power fields, and Ki-67 >20%). In general, patients who have rapidly growing tumors or rapidly progressing extrahepatic disease are not likely to benefit from aggressive surgery. Liver-directed embolic therapy such as bland embolization, chemoembolization, or yttrium-90 (Y-90) microsphere embolization should be considered in these patients [2, 4]. Patients who have slow-growing, indolent disease who have symptomatic tumors, patients who can be resected for cure, patients who have less than 50% of the hepatic parenchyma replaced with tumor in whom we can achieve 70% or better cytoreduction, and patients who have functional tumors are usually considered surgical candidates in our multidisciplinary program. We believe a team approach for decision making is key, as patients often are candidates for multiple forms of therapy not limited to surgical extirpation, including open or percutaneous ablative therapies, minimally invasive ablative therapies or resections, or liver-directed therapies such as chemoembolization or Y-90 microsphere embolization. In general, we do not recommend liver-directed embolic therapy in patients who have had biliary-enteric anastomoses, as they will have a high incidence of intrahepatic abscess formation after embolization. If we know a patient will require liver-directed therapy and biliary-enteric reconstruction as part of either liver resection or pancreatic head resection, we will recommend that the liver embolic therapy should be performed first, followed by subsequent hepatic resection or Whipple procedure. Liver-directed embolic therapy will make the hepatic dissection more difficult, as it engenders intense adhesions between the liver and the surrounding peritoneum. In addition, liver embolic therapy carries with it the risk of gallbladder infarction and acute cholecystitis. We recommend that all patients

Figure 20.9

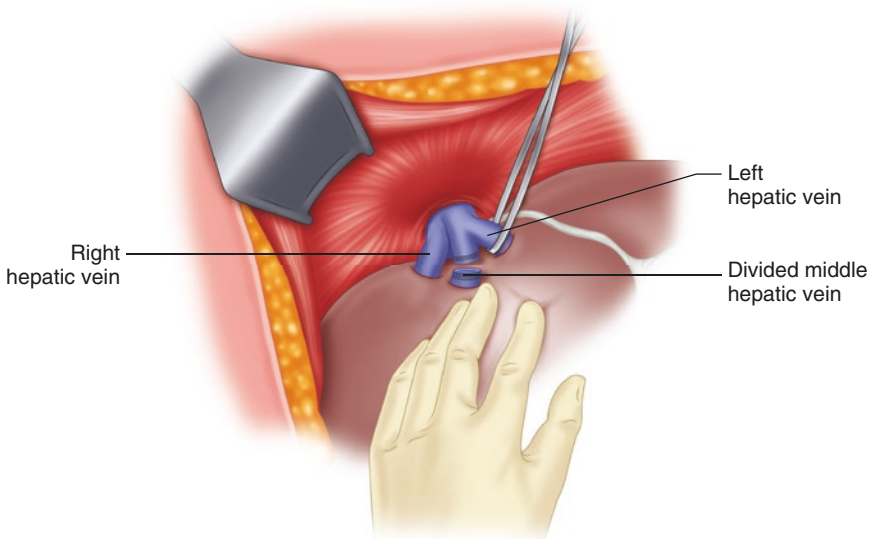


Figure 20.10

Mobilization of the liver off the vena cava

Figure 20.11

Postresection defect with exposed porta hepatis and hepatic veins within the liver

Figure 20.10

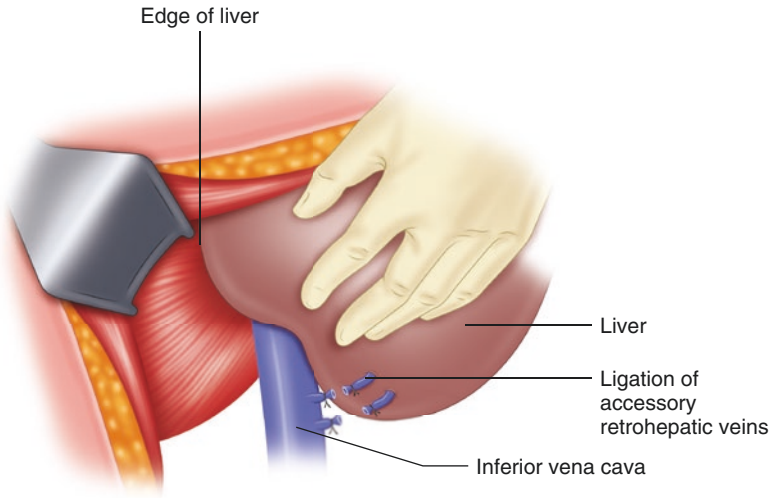
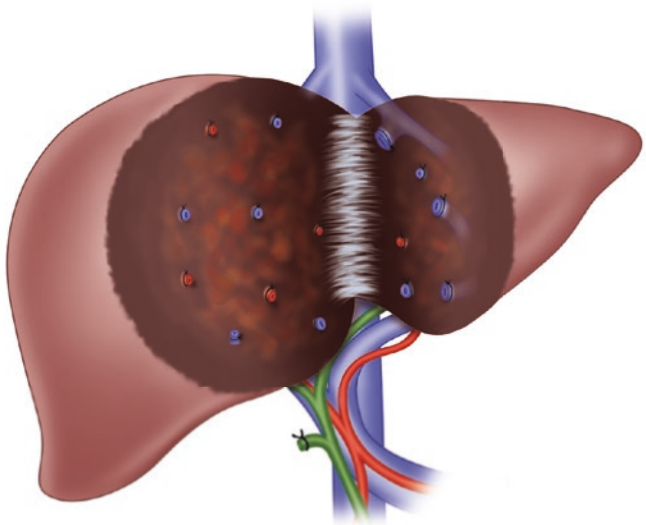


Figure 20.11



who are undergoing surgery should undergo cholecystectomy at the time of surgery if they are on long-term octreotide therapy or will undergo liver-directed embolic therapy. We usually perform liver-directed embolic therapy after all contemplated surgical procedures have been completed, but staging of different therapies is a highly individualized process, which certainly depends on the patient's comorbidities and overall nutritional status. Occasionally, liver-directed embolic therapy can downstage the patient's tumor burden to allow for successful resection, but it will make the mobilization of the liver more difficult. We do employ preoperative right portal vein embolization for diminutive left lobes, to cause hypertrophy of the left lobe. A dedicated team of hepatobiliary surgeons, medical oncologists, nuclear medicine physicians, gastroenterologists, radiologists, and endocrinologists is integral to the decision making process.

In our series of 229 procedures in 189 patients, an aggressive surgical approach has led to long-term survival (87% at 5 years, 77% at 10 years) [5]. In this group of patients with advanced liver disease, whose untreated 5-year survival is generally reported as 30–50%, we agree with others that an aggressive surgical approach is warranted for prolongation and improvement in quality of life [2, 4, 6, 7].

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Wide Excision and Sentinel Node Mapping for Merkel Cell Carcinoma

21

James R. Howe

21.1 Introduction

In 1875, Friedrich Merkel described the cells that bear his name, found within the epidermis and along sweat ducts and hair follicles. These cells are involved in touch reception [1] and are of neuroendocrine lineage, but their origin continues to be an issue of some controversy [2]. Merkel cell carcinomas (MCCs) are tumors that arise from these cells in the dermis; they are usually asymptomatic but may grow significantly over a short period of time. The lesions are red to purple and may appear cystic. They tend to arise in areas of ultraviolet exposure and are often seen in immunocompromised individuals. Most are associated with polyoma virus infection, but the role of polyoma virus in the pathogenesis of MCC is controversial, as antibodies to the virus are seen in up to 50% of the general population. MCC is extremely uncommon in African Americans.

In a large review of the National Cancer Institute's SEER (Surveillance, Epidemiology, and End Results) database, MCC was found to occur more commonly in males (62%), those of white race (95%), and age greater than 70 years (72%). The most common sites of origin were the head and neck (44%), extremities (37%), and trunk (11%). These tumors were localized in 49% of patients, with regional nodal involvement in 31% and distant metastases in 8% [3]. Like melanomas, MCCs are a challenge to the surgical oncologist because of their high rates of local recurrence and regional or distant metastases, with a poorer prognosis than squamous cell or basal cell carcinomas.

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21.2 Operative Details

21.2.1 Wide Local Excision

The basic surgical principles for the treatment of MCC are similar to those for melanoma, except for the fact that MCCs are more radiosensitive than melanomas. In general, the primary tumor should be removed with an adequate margin, and in clinically node-negative patients, the regional lymph nodes should be staged by sentinel lymph node biopsy. If the sentinel lymph node is positive, then a regional lymphadenectomy, irradiation of the nodal basin, or both are recommended [4]. In patients with clinically node-positive MCC, sentinel node biopsy is unnecessary. Instead, confirmatory fine-needle aspiration followed by regional lymphadenectomy and/or irradiation of the nodal basin should be performed [5]. Further descriptions of these formal lymph node dissections and of the controversy regarding the optimal surgical versus radiotherapeutic management of regional nodal basins are beyond the scope of this volume.

The margins of excision in MCC are a point of controversy, and there are no good, randomized studies to guide the surgeon. Given that intradermal dissemination is common and local recurrence is frequently a problem, wider margins should be considered. Using the treatment of melanoma as a guide, margins of 2 cm are reasonable, where possible. If the lesion is on the trunk, an elliptical incision along Langer's lines should be carried out, with 2 cm of clearance from the edge of the lesion laterally along the line; the length along the axis should be three times this width to avoid dog ears (6 cm in each direction from the lesion). If the lesion is on an extremity, the long axis should be oriented in a vertical direction along the axis of the limb (Fig. 21.1).

Once the ellipse is marked, incise the skin through the dermis into the subcutaneous fat. Use electrocautery to divide the fat circumferentially down to the underlying muscle (Fig. 21.2a). It is optional as to whether to remove the fascia of the muscle or leave it intact. Pass off the specimen after marking the superior edge with a short stitch

J.R. Howe (ed.), *Endocrine and Neuroendocrine Surgery*, Springer Surgery Atlas Series, DOI 10.1007/978-3-662-54067-1_21

Figure 21.1

Orientation of incisions of the lower extremity (**a**), upper extremity (**b**), and trunk (**c**)

Figure 21.2

(**a**) Excision of skin and subcutaneous tissue in an ellipse 2 cm from the lesion in the short axis and 6 cm in the long axis. (**b**) Marking of the specimen with a long stitch on the lateral edge and a short stitch on the superior edge

Figure 21.1

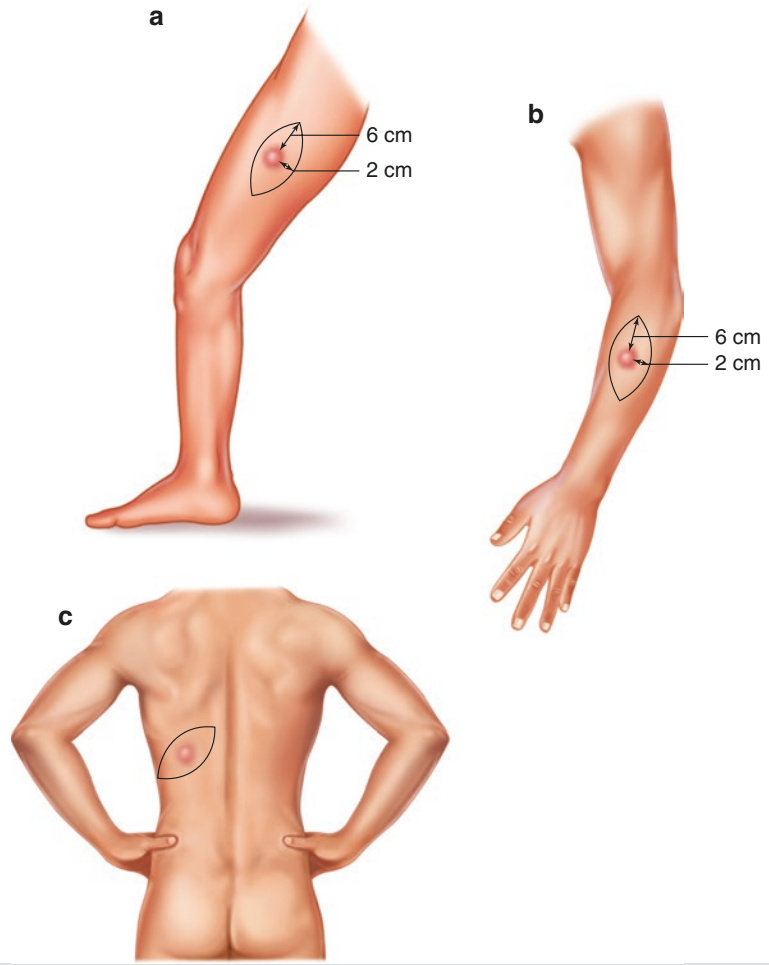
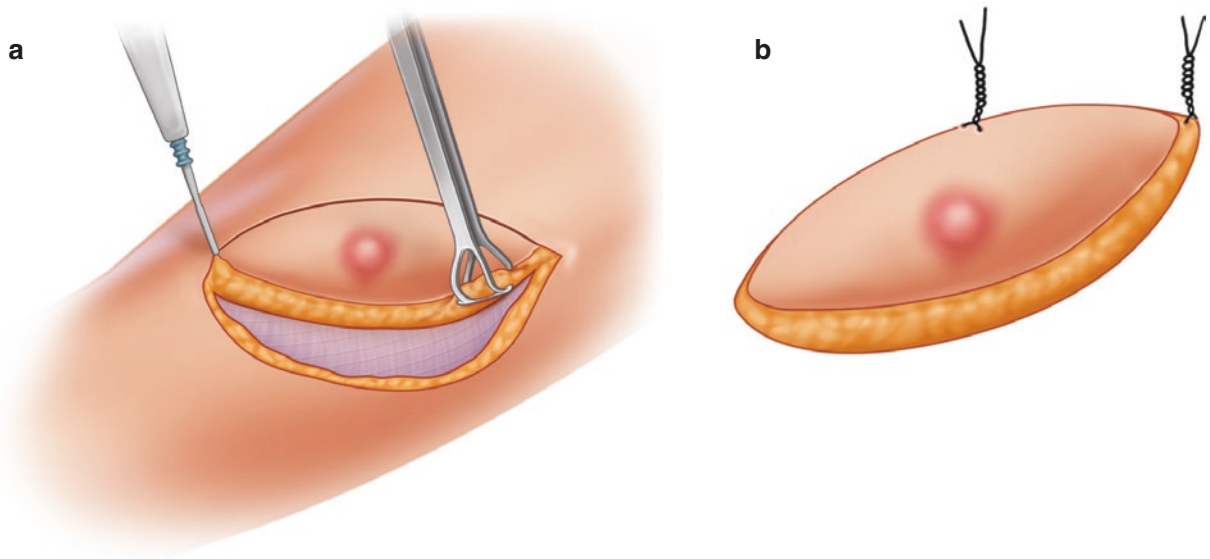


Figure 21.2



and the lateral edge with a long stitch to orient the specimen, in case of positive margins (Fig. 21.2b). Reduce tension by creating flaps, elevating the fat off of the muscle for several centimeters circumferentially. Reapproximate Scarpa's fascia using simple 2-0 or 3-0 Vicryl sutures, placing 6–8 sutures and tagging them with clamps (Fig. 21.3a). Begin tying the sutures at each end, with an assistant pushing the skin edges together as the sutures are tied. If there is a significant depth between Scarpa's fascia and the skin, another layer of simple 3-0 Vicryl sutures may be placed to further close the defect and approximate the subcutaneous wound edges. Place 3-0 nylon vertical mattress sutures spaced at 1-cm intervals through the skin edges (Fig. 21.3b), then tag these with clamps. Begin tying from each edge, with an assistant pushing the skin edges together to reduce tension. If the skin can be brought together with these 3-0 sutures, the wound will heal, but the sutures should be left in place for 2 weeks. There is a tendency for wound edges brought together under significant tension to heal with a thick scar and keloid formation, but most patients find this preferable to the even less cosmetic alternative of a skin graft.

21.2.2 Local Flaps

If cosmesis is a concern, a simple flap may be considered. A rotational flap can be fashioned by drawing a 90° arc from the apex of the defect, then making an incision of several centimeters at a right angle to the base. The tissue is extensively undermined above the level of the muscle fascia, and then rotated into the defect (Fig. 21.4a). Alternatively, a rhomboid flap can be created by making an incision from the edge of the wound for a distance of about three quarters of the width of the wound. Next, an incision of the same length is made from the end of this line at 60°, so that it runs parallel to the wound edge. The tissue between the incisions is freed up from the underlying muscle, keeping the fascia with the flap for improved blood supply. The point at the edge of the wound and the first incision is sutured to the edge of the wound at the opposite side. The point where the two incisions meet is sutured to the apical area of the wound between the first two points, and then the edge of the bottom incision is rotated to the wound edge (Fig. 21.4b). Interrupted nylon sutures are then used to approximate the edges of the rhombus to the circular defect and to close the lateral incision.

Figure 21.3

(**a**) Scarpa's fascia is approximated with interrupted 2-0 Vicryl sutures, then 3-0 nylon vertical mattress sutures are placed but not tied. (**b**) Closure of the skin after tying nylon sutures

21.2.3 Sentinel Lymph Node Biopsy

Patients are brought to the Nuclear Medicine suite prior to their procedure, and 0.5–2 mCi (18–74 MBq) of filtered ^{99}Tc-sulfur colloid is injected intradermally in four quadrants around the base of the skin lesion. This injection is generally done within a few hours of surgery, but good results can be obtained even when it is done 12–24 h prior to surgery. Lymphoscintigraphy is performed with a gamma camera to determine the nodal basins draining from the lesion. For extremity lesions, these will be in the corresponding axillary or inguinal areas, only rarely involving the epitrochlear or popliteal regions for distal extremity lesions. For truncal lesions, the drainage is less predictable, and could involve either or both axillae and/or inguinal regions, or even cervical nodes. If two to three nodal basins show uptake on lymphoscintigraphy, then that part of the skin can potentially drain to any of these nodes, so sentinel nodes will need to be dissected out for all of these nodal basins.

The patient is transported to the operating room, where we prefer the use of general anesthesia. Using a 25-gauge needle, 0.5–3 mL of isosulfan blue dye (Lymphazurin; US Surgical-Tyco; Norwalk, CT, USA) is injected intradermally in four quadrants around the primary lesion (Fig. 21.5a). If the needle is truly in the intradermal space, the injection will be very difficult, and a blue wheal will develop slowly at the injection site; if the dye goes into the skin easily, then it is probably being injected subcutaneously, which may lead to less reliable mapping. Patient positioning will then depend on the site of the primary tumor and the draining nodes; we try not to have to reposition patients, but sometimes it is necessary, especially if multiple drainage basins are seen. We generally perform the sentinel node biopsy prior to excision of the primary to reduce the risk of contamination of the instruments, which may occur if the primary is resected first. In some cases, however, especially when the lesion is very close to a nodal basin, the primary must be resected first so that background levels can be reduced and will interfere less with the node counts.

Before dissection of a nodal basin, a gamma probe (Navigator, Dilon Diagnostics, Newport News, VA, USA; Neoprobe®, Devicor Medical Productions, Cinncinnati, OH, USA; or C-Trak®, Care Wise Medical Products, Brandon, FL, USA) is passed in vertical lines moving from medially to

Figure 21.3

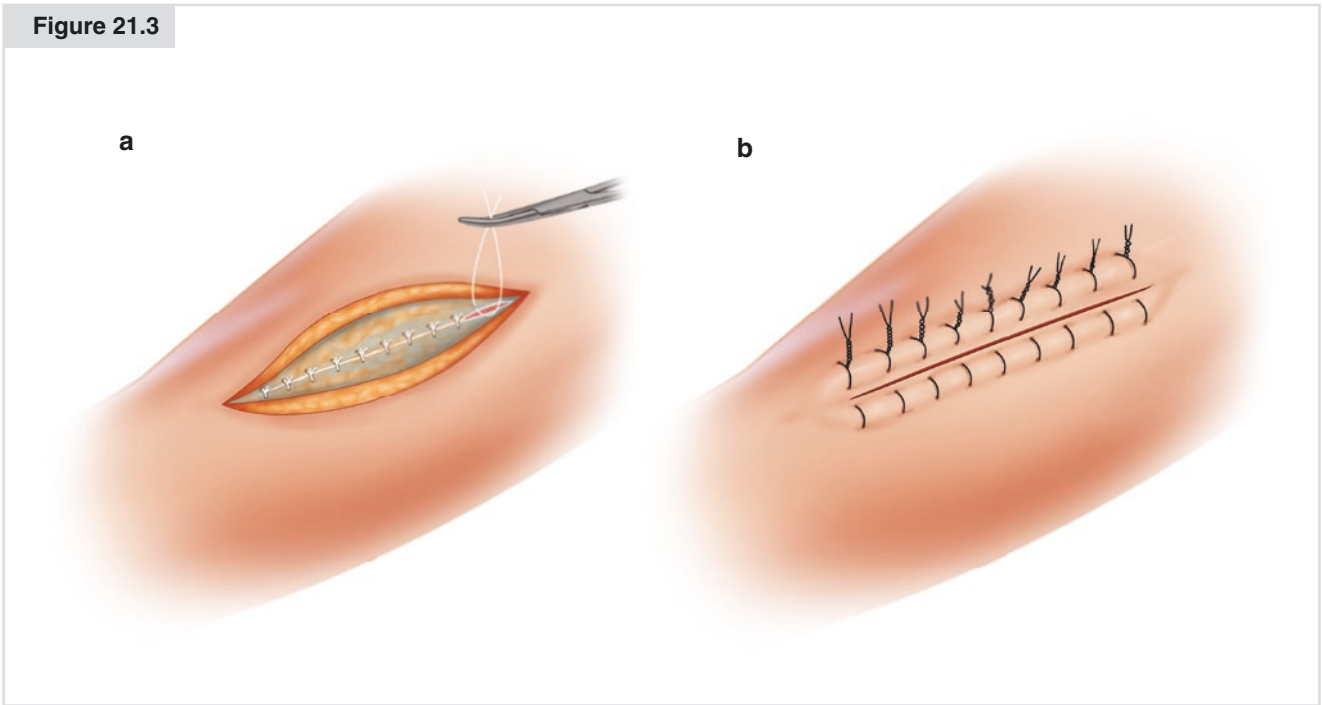
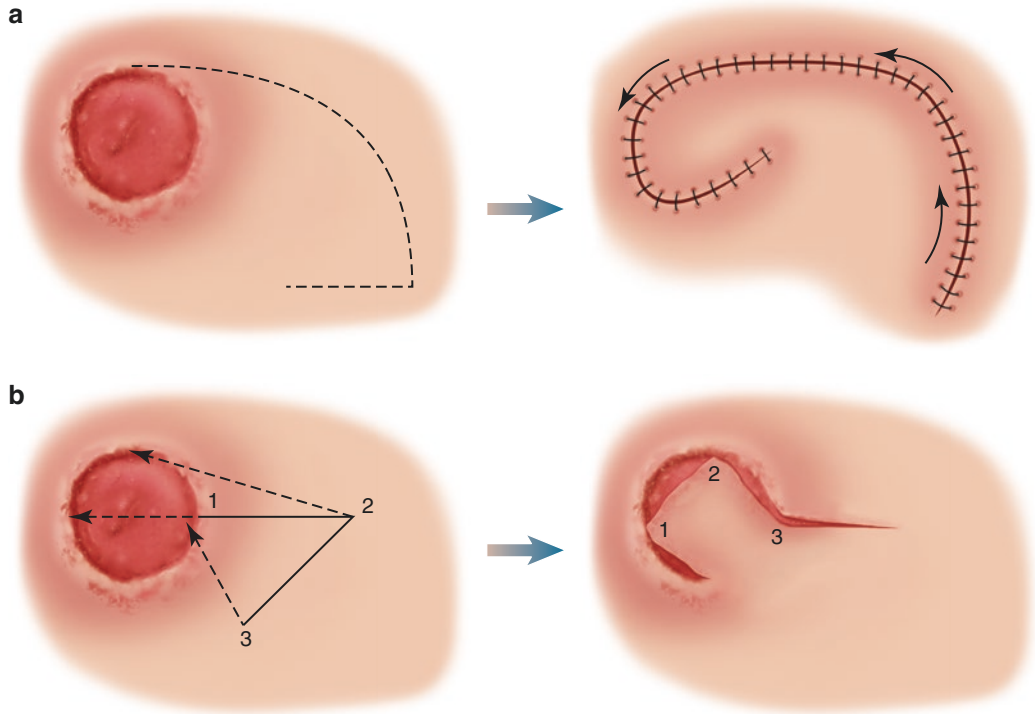


Figure 21.4

(**a**) Rotational flap: a 90° arc is made laterally and then rotated into place. (**b**) Rhomboid flap: an incision is made perpendicular to the edge, slightly smaller than the diameter of the wound; the same length incision is made at 60°. Tissue is extensively undermined, then rotated into the defect as shown. The numbers designate the initial and final positions of the corresponding areas of skin.

Figure 21.4



laterally to determine the site of highest counts, then in horizontal lines inferiorly to superiorly (Fig. 21.5b). The site at which these two areas of highest counts intersect is then marked, and a 10 second count (the pre-excision count) is recorded. Occasionally, lymphoscintigraphy will demonstrate two independent drainage pathways to different nodes (as opposed to one channel traversing a first node and then later appearing in a second node along the same lymphatic channel). When this happens, the two separate nodes should be marked. An incision of 2–3 cm is made over the location of maximal counts (Fig. 21.6a). If this location is in the femoral or inguinal region, the orientation should be vertical or horizontally in a skin crease. These should be oriented so that that if a completion nodal dissection is later carried out, the biopsy site can be encompassed by the lymphadenectomy incision. In the axilla, we generally use an incision that can be encompassed by a future bucket handle incision at the edge of the axillary hairline, when possible.

Once the incision is made, the subcutaneous fat is divided with cautery to a depth of approximately 1 cm. The wound is held open using a self-retaining mastoid retractor; then the gamma probe is placed into the wound. It is aimed in all directions until the area of maximal counts is identified, and a second 10 second count is recorded (in situ count; Fig. 21.6b). Dissection is carried out using a clamp and cautery, dividing the fat in the direction of the node, until a blue node with high counts is seen (Fig. 21.6c). This node is then removed using cautery, and a 10 second count is taken with the node held away from the patient (ex vivo count). Next, the gamma probe is placed back in the wound and aimed in all directions. When the maximal counts are found, then another 10 second count is taken. If this count is 90% less than the pre-excision count or the in situ count, then this nodal basin is finished. If counts remain above this level, it is likely that there is another sentinel node, which should be sought out and removed in similar fashion. After ensuring adequate hemostasis, the subcutaneous layer is reapproximated with one or two 3-0 Vicryl sutures and the skin is closed with a 4-0 Monocryl subcuticular stitch. Surgical glue is applied over the incision.

Figure 21.5

(**a**) Intradermal injection of isosulfan blue dye (Lymphazurin) in four quadrants around the primary lesion. (**b**) Passage of the gamma probe vertically and horizontally to define the area of highest counts

21.3 Results and Follow-Up

Patients return to the clinic for removal of sutures from the primary lesion in 2 weeks. If pathologic examination reveals a close or positive margin, then a re-excision may be necessary. If the sentinel node contains metastatic MCC, then a completion nodal dissection or radiation of the regional nodes is indicated. Depending on the location of the involved node, this procedure would involve an axillary dissection, a superficial and/or deep inguinal node dissection, or potentially a modified neck dissection. It is advisable to perform an ^{18}FDG-PET scan prior to the regional node dissection to rule out distant metastases. The presence of such metastases may argue against further lymphadenectomy, especially in elderly or immunosuppressed patients. If the patient presents with palpably enlarged nodes that are positive on fine-needle aspiration, then a regional nodal dissection, regional irradiation, or both should be performed instead of a sentinel node biopsy. A PET scan would be recommended prior to the procedure to rule out distant disease.

In the SEER database, 10-year survival rates were 71% for patients with localized disease, 48% for those with regional disease, and 20% for those with distant disease [3]. In a series of 251 patients from Memorial Sloan-Kettering Cancer Center, recurrence was seen in 102 (43%) of 237 patients presenting with localized or regional disease, within a median of 9 months. Distant metastases were ultimately seen in 21% of patients presenting with locoregional disease. Factors significantly associated with improved survival were head and neck site, tumor size less than 2 cm, use of chemotherapy, the absence of lymphovascular invasion, and clinical nodal status (which was the only factor significant by multivariate analysis) [6].

Treatment of local recurrence is re-excision, radiotherapy, or both. Distant recurrences are commonly associated with local recurrence, and one should consider performing a PET scan if local recurrence is found. Metastatic disease or troublesome locoregional recurrence can be quite chemosensi-

Figure 21.5

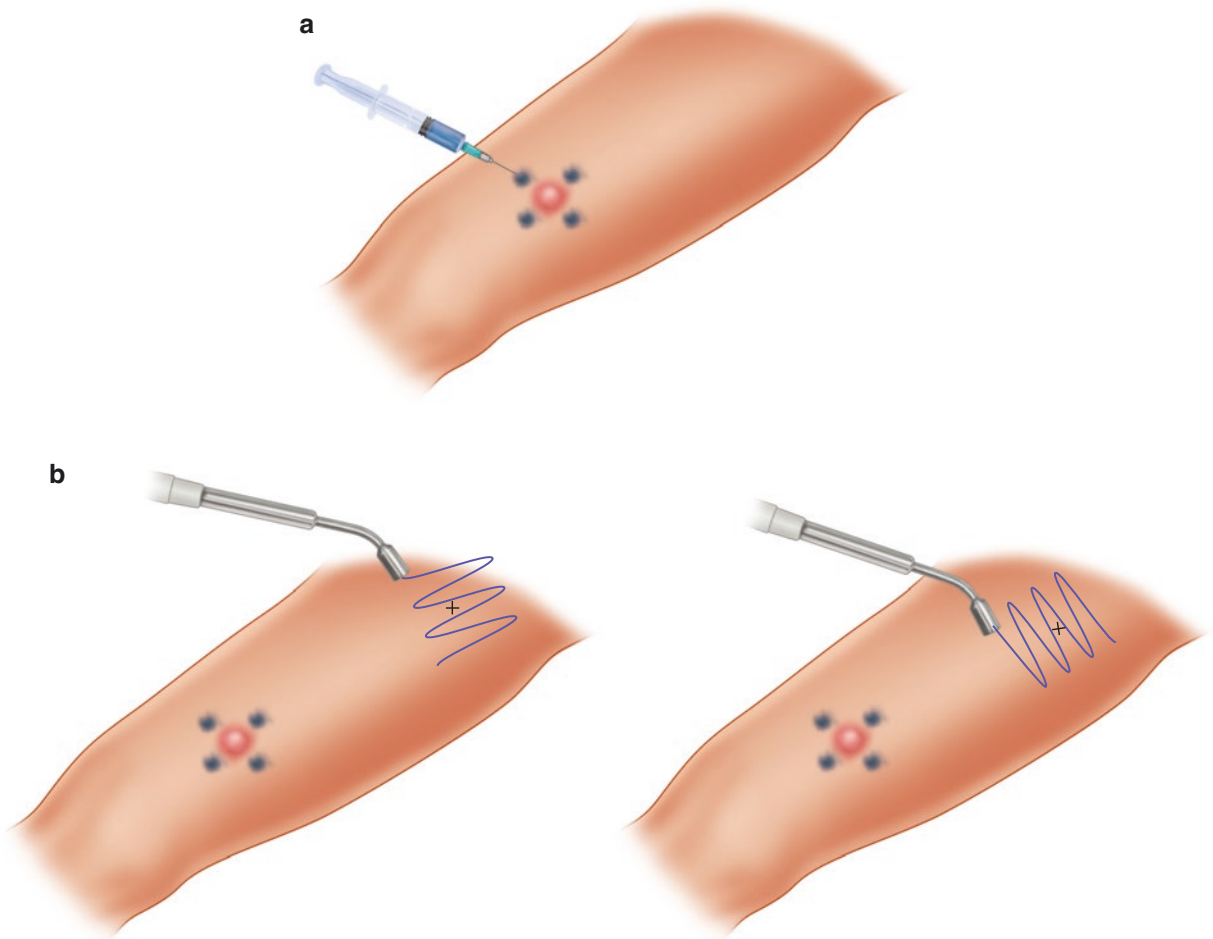
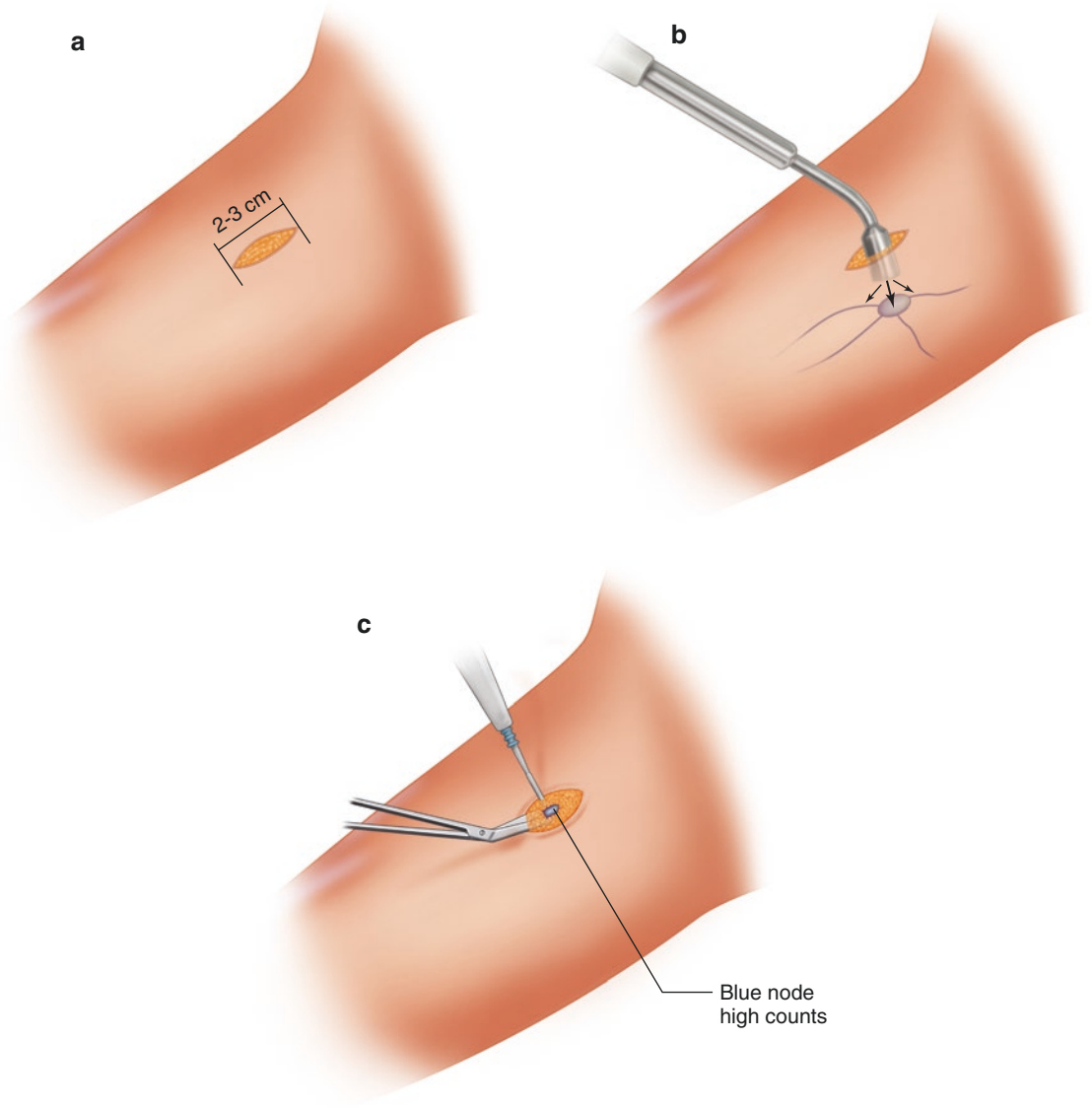


Figure 21.6

(**a**) A skin incision 2–3 cm in length is made over the site of maximum counts, oriented along the extremity (or Langer's lines, if in the head and neck or trunk). (**b**) In situ counts are taken to determine the direction and depth of dissection. (**c**) Subcutaneous dissection is carried out until a blue node with high radioactivity is found

Figure 21.6



tive. Various chemotherapy regimens (such as those used for small cell carcinomas) are used, but responses typically last less than a year [2].

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