REVIEW



# Thoracic sympathectomy: a review of current indications

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#### Abstract

*Background* Thoracic sympathetic ablation was introduced over a century ago. While some of the early indications have become obsolete, new ones have emerged. Sympathetic ablation is being still performed for some odd indications thus prompting the present study, which reviews the evidence base for current practice.

*Methods* The literature was reviewed using the PubMed/ Medline Database, and pertinent articles regarding the indications for thoracic sympathectomy were retrieved and evaluated. Old, historical articles were also reviewed as required. *Results and conclusions* Currently, thoracic sympathetic ablation is indicated mainly for primary hyperhidrosis, especially affecting the palm, and to a lesser degree, axilla and face, and for facial blushing. Despite modern pharmaceutical, endovascular and surgical treatments, sympathetic ablation has still a place in the treatment of very selected cases of angina, arrhythmias and cardiomyopathy. Thoracic sympathetic ablation is indicated in several painful conditions: the early stages of complex regional pain syndrome, erythromelalgia, and some pancreatic and other painful abdominal pathologies. Although

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ischaemia was historically the major indication for sympathetic ablation, its use has declined to a few selected cases of thromboangiitis obliterans (Buerger's disease), microemboli, primary Raynaud's phenomenon and Raynaud's phenomenon secondary to collagen diseases, paraneoplastic syndrome, frostbite and vibration syndrome. Thoracic sympathetic ablation for hypertension is obsolete, and direct endovascular renal sympathectomy still requires adequate clinical trials. There are rare publications of sympathetic ablation for primary phobias, but there is no scientific basis to support sympathetic surgery for any psychiatric indication.

**Keywords** Sympathectomy · Thoracoscopy · Hyperhidrosis

The indications for sympathetic ablation have evolved since Alexander first performed this operation in 1889 to treat epilepsy [1]. Jonnesco [2] and Jaboulay [3] extended its application to the treatment of exophtalmic goitre. François-Franck [4] reported its use for the treatment of glaucoma, idiotism and hyperthyroidism. These indications became obsolete long ago. However, even currently, sympathetic surgery is performed and reported for some odd indications. The present review was undertaken in order to examine the evidence base for the indications currently in use. The older open methods have given way to endoscopic techniques, but this review is concerned with the indications for sympathectomy, techniques of which will not be discussed in detail.

# Methods

Search of the literature was performed in the PubMed/ Medline Database for the years 1990–2014 (the period in which the endoscopic approach of sympathetic ablation supplanted open surgery). To identify the indications in current use, an initial search was made using as terms "Indications" AND "Thoracic Sympathectomy OR Sympathicotomy OR Sympathetic ablation" NOT "Renal Sympathectomy". During the complete retrieval process, some additional rare indications were identified and included in the present review. This was followed by individual searches in the Database for each indication, using as terms the pathology, e.g. "Palmar hyperhidrosis" AND "Thoracic Sympathectomy OR Sympathicotomy OR Sympathetic ablation". To focus on the subject, exclusion of similar pathologies was added to the search items (e.g. for the search of palmar hyperhidrosis "NOT Axillary hyperhidrosis" was added). Review articles and clinical trials were sorted out. Selection of studies was made in three steps: (a) by the relevance of the title; (b) by scrutinizing the abstracts of articles selected in the first stage; and (c) by scrutinizing the full text of articles selected in the second stage. All review articles and clinical trials were scrutinized according to the same three steps. Older publications were retrieved as appropriate.

# Results

The search of the literature for current indications of thoracic sympathetic ablation yielded 68 articles. Step one selection (by titles) restricted the list to 31 and a further selection (step 2, by abstracts) restricted the list to 14 publications. The following current indications were identified in current use for performing thoracic sympathectomy: hyperhidrosis—palmar, axillary and facial (craniofacial); blushing; cardiac indications; pain conditions; ischaemia; and psychiatric conditions. For hypertension, renal sympathectomy has supplanted thoracic sympathetic ablation. The figures of retrieved articles for each indication are listed in Table 1. A paucity of clinical trials is noticeable. Randomized trials and reviews based on randomized trials are extremely rare. Articles pertinent to such studies are outlined in the discussion.

## Discussion

## Hyperhidrosis

Hyperhidrosis is excessive secretion from the eccrine sweat glands [5]. Most cases are primary, of unknown aetiology, but a few may be secondary to other disorders [6]. Hyperhidrosis can cause severe social, emotional and occupational handicaps from an early age. Many treatments have been proposed [7, 8], but the only one which may abolish palmar hyperhidrosis is sympathetic ablation [8].

The first sympathetic ablation for hyperhidrosis was performed by Kotzareff [9] and reported in 1920. Since that publication, thoracic sympathetic ablation became widely used for palmar overperspiration, and later extended for axillary and facial hyperhidrosis.

## Primary palmar hyperhidrosis

Primary palmar hyperhidrosis (PHH) is currently the major indication for upper thoracic sympathectomy. An exhaustive review in 2000 [8] has shown that resection of the T2 and T3 ganglia invariably results in palmar anhidrosis. It has been proven that quality of life of patients with PHH is substantially improved by sympathetic ablation [10], and improved quality of life remains stable in the long term [11]. Furthermore, according to patients' subjective evaluation, the worse pre-sympathetic ablation quality of life resulted in the best quality of life estimation following the procedure [12]. Nevertheless, surgery is still controversial because of the risk of compensatory hyperhidrosis-excessive sweating developing in areas unaffected by the sympathetic ablation—often resistant to treatment [13], and which may be very debilitating [14]. Performing a preoperative chemical sympathetic block was suggested as a method to evaluate the probability of developing compensatory hyperhidrosis following surgical sympathectomy [15]. To reduce the degree and occurrence of compensatory hyperhidrosis, a multitude of technical variations have been suggested [13], but published recommendations are often contradictory. There is an enormous bulk of literature dealing with this question. While many studies advocate that lowering the level of ablation (from T2 to T3 or T4) [16–18] or restricting the extent of ablation reduce the severity and incidence of compensatory hyperhidrosis [19], other studies contradict these claims [16, 20-22]. Two recent reviews published in 2011 underline this controversy. In a "consensus for the treatment of hyperhidrosis" based on a review of randomized studies, a group of authors suggested ablation at the upper level of the third rib (a presumably T3 ablation) as the best procedure for PHH [23]. Another simultaneously published systematic review and meta-analysis of the literature suggested that T3 ablation alone resulted in a significantly higher degree of compensatory sweating than T2-T4 sympathectomy [24], recommending the latter approach. Although there is no agreement, it appears that lowering the level of sympathetic ablation and limiting its extent reduces compensatory hyperhidrosis, but the amount of achieved reduction in palmar sweating is lower as well [25-27], and the percentage of recurrences of PHH is increased [13]. Due to the risk of compensatory hyperhidrosis and other late side effects [28], and possible early complications [29-31], sympathetic ablation should be restricted to those whose

 Table 1
 Results of the literature search

Indication	Articles obtained by the search			Articles retrieved by:	
	Total #	Reviews	Clinical trials	Title	Abstract
Hyperhidrosis					
Palmar	502	36	61	65	55
Axillary	67	14	8	18	9
Facial (Craniofacial)	164	20	12	17	12
Blushing	22	4	2	13	13
Cardiac indications					
Angina	51	6	4	22	10
Arrhythmias					
Ventricular tachycardia	58	8	2	5	2
Long QT syndrome	61	17	0	10	6
Cardiomyopathy	41	4	5	5	3
Pain conditions					
Complex regional pain syndrome	45	4	1	18	9
Erythromelalgia	11	2	0	2	1
Pancreatic and splanchnic pain	43	9	2	10	5
Ischaemia					
Atherosclerosis	7	1	0	2	2
Thromboangiitis obliterans	37	2	0	4	3
Raynaud's phenomenon	77	9	4	9	3
Scleroderma	34	8	2	8	4
Rheumatoid arthritis	7	0	0	1	1
Lupus erythematosus	4	0	0	1	0
Paraneoplastic syndrome	3	1	0	2	1
Microemboli	1	0	0	1	1
Frostbite	9	4	1	4	3
Vibration syndrome	4	1	0	3	3
Hypertension	1	0	0	0	0
Psychiatric indications (phobias)	8	2	1	6	6

quality of life is severely affected. The surgeon should be well aware of the various procedures and their expected results, and discuss the operation with the patient in order to obtain a truly informed consent for the operation.

Failures of sympathetic ablation for PHH may be to due either an incomplete or inadequate ablation of the correct sympathetic segment (occurring early after the initial operation), or a true recurrence (developing months or years after the initial operation), probably due to nerve regeneration or sprouting of nerve fibres from the injured sympathetic chain [32]. Resympathectomy has been reported to be beneficial for both types of recurrent overperspiration [33, 34]. However, both surgeons and patients should be aware that repeat ablation may increase the occurrence of compensatory hyperhidrosis [34, 35].

There is a multitude of non-surgical procedures in the treatment of PHH [8, 36]. None of them secures permanent cure. Therefore, their use may be attempted in milder cases of PHH. However, for patients with disabling PHH,

sympathetic ablation remains the only method of treatment which may produce permanent and complete relief of palmar overperspiration and should be regarded as first-line treatment [37]. Due to the potential side effects of sympathectomy, patients should be well informed of these limitations before embarking on the procedure.

# Axillary hyperhidrosis

Axillary sweating may accompany PHH but isolated axillary hyperhidrosis (AHH) is also encountered. Severe isolated AHH also affects the quality of life and impinges upon the daily social and working interactions of the patient. Sympathetic ablation may alleviate the condition. However, in the era of open surgery, AHH was not considered as a primary indication for sympathectomy, excision of the axillary skin being a simpler and effective procedure [38, 39], despite the drawback of poor healing and an unsightly scar. The advent of endoscopic surgery simplified the operative procedure and AHH became one of the indications for sympathetic ablation. It has been shown that sympathectomy for AHH should be at a lower level of ablation than for PHH [40–42], going down to T4–T5 [40, 41], and in 2008 satisfactory results have been published in a randomized controlled study [42]. However, analysis of one of the largest published series [43] has shown that, compared to the results for palmar hyperhidrosis, the results for AHH are worse: the percentage of totally satisfied patients was lower, the percentage of dissatisfied patients was double, and the percentage of those regretting the operation was 4.5 times higher for AHH than for PHH.

Restricting the indication for sympathetic surgery for AHH is also due to the existence of several local nonsurgical and surgical options which may alleviate excessive perspiration. Local treatments include antiperspirants, iontophoresis and Botox-A injections. Non-surgical local treatment of the perspiring area by microwaves has been reported to achieve substantial reduction in axillary sweat [44]. Local surgery includes subcutaneous curettage, either with a curette [45] or by suction [46], which has also been stated to be successful in a high percentage of cases. Successful treatment of AHH by excision of the axillary skin, either partial [47] or complete [48], has also been advocated. A recent comparative study has shown that local excision yields superior results than sympathetic ablation for AHH [49], practically avoiding the sequel of compensatory hyperhidrosis.

When the axilla is an isolated area of overperspiration, local treatment may be sufficient and satisfactory. Sympathetic ablation for AHH should be therefore restricted only to patients whose AHH is concomitant with PHH. This restricted indication seems to be at present the gold standard for sympathetic ablation in cases of AHH.

## Facial hyperhidrosis

The reported incidence of facial hyperhidrosis varies tremendously. Some publications claim it is very frequent while others hardly mention it. One dermatological study reported that facial hyperhidrosis accounted for 5% of patients who seek help for overperspiration [50], and another report stated that facial hyperhidrosis was the most frequently affected site [51]. In a sympathetic surgical study, facial hyperhidrosis (including blushing) was the indication in 10 % of 650 procedures [52], while in an Asian study, facial hyperhidrosis was seen in just one of every 40 patients who suffered from palmar hyperhidrosis [53]. Facial hyperhidrosis should be distinguished from Frey's Syndrome, a frequent sequela of parotidectomy, in which gustatory stimuli result in facial sweating or blushing, and for which sympathetic surgery should not be considered.

Several, non-surgical treatment modalities have been suggested for facial hyperhidrosis, including oral medications (glycopyrrolate and clonidine), topical medications and botulinum toxin injections [36].

Due to the possibility of developing Horner's syndrome and compensatory hyperhidrosis, sympathetic ablation is considered the last-line of treatment [36]. Yet, and although rarely reported, thoracoscopic sympathetic ablation for isolated facial hyperhidrosis is effective [36, 43, 52–56]. Ablation is directed at the higher levels of the sympathetic chain, which is considered necessary to achieve an effect in the face. The most common surgical intervention is R2 (rib) sympathicotomy, but reports include R2–R3 sympathicotomy [43], G2 (ganglion) ramicotomy [44], G2 ablation [52] and even clipping of the lower part of the stellate ganglion without causing any Horner's syndrome [56].

#### Blushing

Normally, reddening of the face is part of a physiologic thermoregulatory response to hyperthermia that results from increased cutaneous blood flow caused by transient vasodilatation. This may also be triggered by multiple conditions which have been reviewed extensively [57]. Blushing is triggered by emotion and should be distinguished from flushing which appears as a symptom of underlying somatic disease. In severe cases, blushing is often associated with a feeling of embarrassment, and some individuals may experience so much distress that they develop a phobia about it [58]. The exact nature of this vasomotor phenomenon is unclear and the prevalence is unknown, but the incidence varies with geographical location. However, due to the emotional nature of the phenomenon, psychotherapeutic approaches have been considered [59] in addition to local [60] and systemic pharmacotherapies [61]. In a recent review of available treatments [62], the authors considered sympathetic ablation to be the most appropriate treatment of blushing.

Thoracoscopic sympathetic ablation for facial blushing was first described in 1985 [63], but the number of papers on this subject is much lower compared to those for primary hyperhidrosis [43, 52, 64–85]. In Scandinavia, surgical treatment of blushing accounted for approximately half of all sympathectomies [77, 85], whereas sympathetic ablation for this indication is quite rare in Asia [68]. The reason could be either a different cultural attitude to the problem or, possibly, a true constitutional difference between populations.

There is no consensus on the extent or level of sympathetic ablation for isolated facial blushing, which has been targeted at R1–R3 [65], R2 [52, 73], R2–R3 [18, 25, 63, 75, 76], R2–R4 [70], R2–R5 [64, 71] or R3–R4 [18]. However, a recent randomized clinical study [85] comparing R2 versus R2–R3 sympathetic ablation did not show any significant difference in local effect.

Results from the literature indicate that sympathetic ablation for facial blushing is effective, but meticulous and critical patient selection is essential and thorough information about the high risk of side effects is crucial. In general, complications and side effects following sympathetic ablation for isolated facial blushing are similar to those seen after sympathetic surgery for primary hyperhidrosis [29]. Compensatory sweating is the most commonly reported side effect, seen in almost all patients treated for facial blushing [18, 43, 44], and gustatory sweating is observed post-operatively in one-third of patients [36]. However, contrary to sympathetic surgery for palmar and axillary hyperhidrosis, the risk of Horner's syndrome is increased when sympathetic ablation is performed for blushing, because the sympathetic chain is approached at the level of the second rib, which is considered essential to achieve an effect in the face. Blushing must be of major concern to the patient, enough to tolerate a substantial amount of compensatory sweating after the operation as well as gustatory sweating. It should also be kept in mind that upper chest or neck blushing as well as a slowly emerging and long-lasting facial flushing respond poorly to sympathetic surgery.

# **Cardiac indications**

Sympathetic surgery has now very little place in the management of cardiac conditions, but a few indications remain.

#### Angina

The possible use of sympathetic ablation to treat angina was suggested by François-Franck [4], based on his studies and the understanding of the afferent sympathetic pathways. Cervical sympathetormy for cardiac indications was performed as early as the 1920s with positive results [86]. Although sympathetic ablation results in vasodilatation, the effect of this procedure on pain is attributed to interruption of significant pain pathways from the heart and not to improvement of cardiac perfusion [87, 88].

With the advent of coronary surgery and endovascular procedures, one might expect that sympathectomy for angina would become obsolete, but sporadic cases of noncompliant coronary artery spasm successfully treated by T2 to T4 sympathetic ablation are being published, remaining a useful tool in the treatment of the very selected cases of refractory angina [66, 67, 89]. A preliminary stellate sympathetic block may confirm the efficacy of the procedure prior to surgery [90]. However, the haemodynamic instability of these patients remains a concern when considering surgery.

#### Arrhythmias

In the late 1970s and early 1980s, Schwartz [91] experimentally demonstrated the influence of the autonomic nervous system on cardiac electric activity. The role of the left and right cardiac sympathetic nerves has also been elucidated by the addition of right cardiac sympathetic ablation to left cardiac sympathetic denervation in managing cardiac dysrhythmia [92]. Presently, the role of the autonomic nervous system in modulating cardiac electrophysiology and arrhythmogenesis [93] is well established and justifies sympathetic ablation for the treatment of arrhythmias in appropriate conditions.

Ventricular tachycardia: The medical treatment of 1. arrhythmias is by beta-blockers or by implanted cardioverter-defibrillators for refractory cases. Yet, in a small percentage of patients, ventricular tachycardia refractory to traditional therapies (so-called electrical storm) is encountered [94]. For decades, it has been accepted that the sympathetic nervous system has profound and recurrent effects on cardiac electric activity [95, 96]. Based on this concept, Estes and Izlar [97] performed bilateral stellectomy in the 1960s, in an attempt to treat ventricular arrhythmias. In 1968, Zipes et al. [98] reported a successful case of bilateral stellectomy in conjunction with atrial pacing in a patient who had malignant ventricular arrhythmias. Sympathetic ablation, performed in the rare cases with ventricular tachycardia irresponsive to conventional therapy, with substantial success was reported as recently as 2012 [92] and 2014 [99]. Bilateral ablation may give superior results than left sympathectomy alone [99].

Two recent publications, one animal [100] and one human study [101], examined the effect of renal denervation on ventricular arrhythmias. Due to the relative ease in performing endovascular renal denervation, when indicated, this technique may possibly supplant in the near future the use of thoracic sympathectomy in the treatment/prevention of ventricular tachycardia.

2. Long QT syndrome (LQTS): LQTS is a hereditary disorder characterized by a prolonged QT interval and a polymorphic ventricular tachycardia, leading to severe events: syncope, cardiac arrest, and sudden death [102]. There are eight forms of congenital LQTS in which gene mutations cause potassium, sodium and calcium ion channel disorders [103, 104]. In a recent review, the treatment of LQTS was delineated to

consist of  $\beta$ -adrenergic blocking agents, cardioverterdefibrillator implantation and sympathetic ablation [105]. Moss and McDonald [106] in 1971 reported their pioneer work of successfully treating long QT syndrome with left cardiac sympathetic ablation. In humans, left cardiac sympathetic ablation. In humans, left cardiac sympathetic malignant thereby diminishes the probability of malignant arrhythmias [104]. In 2004, a group of 147 patients with LQTS who underwent sympatheticmy were reported [107]. Almost half of them were free of symptoms post-operatively and on long-term followup. In the remaining individuals, the occurrence of cardiac events decreased substantially. These results illustrate the value of sympathetic surgery for LQTS.

## Cardiomyopathy

The treatment of cardiomyopathy is medical. Patients with heart failure due to cardiomyopathy are not good candidates for surgery, yet sympathectomy has been attempted in order to improve their cardiac performance. In a study of patients with dilated cardiomyopathy, a high thoracic sympathetic ablation significantly reduced the left ventricular cavity, boosting the ejection fraction, and thus improving the left ventricular diastolic function [108]. The same results were obtained in a controlled study published in 2010, and improvement persisted at 6-month follow-up [109]. A later study, further confirmed that left ventricular function in patients with dilated cardiomyopathy is improved by sympathectomy [110]. Thus, it may be concluded that sympathetic blockade has a place as an adjunctive therapy in selected patients with severe dilated cardiomyopathy.

## Pain conditions

Sympathetic ablation may be indicated for a few painful conditions.

# Complex regional pain syndrome

This is an out of proportion, bizarre, and poorly understood painful response triggered by trauma to a limb. It causes allodynia (the perception of a non-painful stimulus as painful) and hyperpathia (an exaggerated pain response to a painful stimulus). Sympathetic dysfunction, usually overactivity, becomes evident. Varying trophic changes can follow and eventually the condition may lead to irreversible severe incapacity.

Synonyms include causalgia, post-traumatic sympathetic dystrophy, reflex dystrophy, Sudek's atrophy, posttraumatic dystrophy, shoulder-hand syndrome, post-traumatic pain syndrome, sympathetic neurovascular dystrophy, post-traumatic spreading neuralgia, to mention just a few [111]. However, because the role of the autonomous nervous system is obscure in the pathogenesis of these disorders, the term "Complex regional pain syndrome" (CRPS) is preferred. CRPS is subdivided into two groups: I—following tissue trauma and II—following trauma to a nerve [112]. The pathogenesis is obscure. A regional inflammatory response to the initial trigger has been implicated [113, 114]. Clinical findings suggest that patients with CRPS have autonomic dysfunction within the central nervous system [115].

There is very little good evidence in the literature to guide treatment of CRPS. Early recognition and a multidisciplinary approach to management seem important in obtaining a good outcome. Treatments aimed at pain reduction and rehabilitation of limb function form the mainstay of therapy. Bisphosphonate-type compounds and steroids have been used as pharmacotherapy, with some beneficial effect [116]. Emerging data indicate a possible role of inflammation in the overall pathophysiology and have led to treatment with anti-inflammatory medications [117] and steroids. Numerous other oral drugs, including muscle relaxants, benzodiazepines, antidepressants, anticonvulsants, and opioids, have been reported on anecdotally [116]. Behavioural therapy, physiotherapy or occupational therapy is also reported in the armamentarium of CRPS treatment, possessing a potential beneficial effect [118]. Invasive treatments, including nerve blocks, intraspinally administered drugs and neuromodulatory therapies like spinal cord stimulation have all been attempted, but no definite treatment has been established [116].

Due to the possibility of sympathetic overactivity, sympathetic ablation has been used to treat CRPS as well. This concept has been validated in an animal study aimed to determine the effect of sympathectomy on allodynia and heat hyperalgesia produced by a prior L5 and L6 spinal nerve ligation [119]. In a human study, overactivity of the sympathetic system has been demonstrated as well [120]. Yet, two systematic reviews [121, 122] detected only uncontrolled studies and reports of personal experience, and some authors advocated that sympathectomy should be avoided in the treatment of CRPS [123]. Nevertheless, the use of sympathetic ablation in patients with CRPS is repeatedly published. Chemical sympathetic blocks have been successful [124] as well as permanent sympathetic denervation achieved by surgery [120, 125–130]. Even in cases with block failure, sympathectomy may still succeed [102]. Good reported results are as high as 94 % [126]. A meta-analysis of 1528 collected cases of causalgia [131] published in 2003 considered most cases to be cured by

surgical sympathectomy. However, it seems necessary to perform the ablation early in the course of CRPS as with time it becomes independent of sympathetic activity [132]. The level of sympathetic ablation performed has varied between the stellate ganglion down to T7 [100], but more recently the stellate ganglion has not been included, and the usual level in use was restricted from T2 only [129] to T2–T3/T4 [128]. Finally, it may be of interest to report an anecdotal case in which sympathetically maintained pain which recurred after sympathectomy was relieved by the addition of contralateral sympathetic innervation [133].

Until systematic controlled studies are performed, the present data allows cautious use of timely sympathetic ablation in properly selected patients.

#### Erythromelalgia

Erythromelalgia is a rare syndrome of unknown aetiology, characterized by episodes of burning pain, redness, oedema and increased temperature in the upper, lower or both extremities [134]. SCN9A gene mutation has been identified in some but not in all patients [135]. Patients with erythromelalgia without SCN9A gene mutation seem to be more refractory to treatment [135]. Erythromelalgia may be primary or secondary to several conditions, and microvascular arteriovenous shunting has been implied [136]. Several drugs have been used in its treatment, aspirin being foremost [136]. A neurophysiologic study has shown another pathology: distal small-fibre neuropathy with selective involvement of cutaneous sympathetic fibres [137]. Based on this finding, sympathetic ablation has been used in the treatment of erythromelalgia, but the reported cases are scanty. Both failure [138] and success [134, 135, 139] have been reported.

# Pancreatic pain and other painful abdominal pathologies

Sympathetic ablation has been reported as beneficial for abdominal pain. The main indications are pancreatic pathologies (cancer or chronic inflammation) [140], but also adrenal metastases [141], and other abdominal malignancies as validated in a recent prospective multicentral trial [142]. Sympathetic ablation has been used as well in the treatment of intractable abdominal pain due to other pathologies, such as portal vein thrombosis [143].

Splanchnicectomy is the usual procedure [140, 141, 143–149]. The technique includes transection of the post-ganglionic sympathetic nerve branches which unite to create the greater and the lesser splanchnic nerves. However, addition of sympathetic chain ablation has also been reported. Kusano et al. [144] performed a T5 to T9 chain resection/electrocoagulation, whereas Lönroth et al. [143] divided the sympathetic chain and splanchnic branches from T4 down to T10-11. Although a bilateral approach has been advocated [140, 145, 146], some authors [144-149] recommended a unilateral approach, according to the location of the abdominal pain, reserving the bilateral approach only for diffuse abdominal pain. If pain recurred, a contralateral additional splanchnicectomy was performed. The endoscopic approach is invariably used. The timing of the operation in relation to other treatments seems to be important. Howard et al. [146] were impressed that splanchnicectomy appeared to work best in patients who have had no prior operative or endoscopic intervention. Isa et al. [150], in a systematic review published in 2014, reported that pre-operative opioid use was associated with a worse outcome after thoracoscopic splanchnicectomy in patients with chronic pancreatitis. Similarly, Amr and Makharita [142], in their prospective randomized multicentre study of patients with inoperable abdominal or pelvic cancer, found that early sympathetic ablation obtained better results than in patients operated on after opioid treatment had failed.

When performed for pain due to malignancy, the results are good because survival is short. When performed for chronic pancreatitis, results of splanchnicectomy are variable. Short-term results are almost invariably good [141, 146, 149]. Studies with long-term follow-up reported variable outcomes. Stone and Chauvin [149], in their series of alcoholic pancreatitis patients, reported persistent relief with a mean follow-up of 16 months. However, in this study, a bilateral truncal vagotomy had been added to the sympathetic procedure. The role of additional vagal ablation has not been elucidated, and further appropriate studies are required. Kusano et al. [144] reported pain relief at a 13.7-month mean follow-up in two-thirds of patients only. In the study of Buscher et al. [145], only a 50 % long-term persistent pain relief was reported, whereas Maher et al. [148] reported only temporary improvement in most patients.

#### Ischaemia

In the past, sympathectomy was used extensively for ischaemic disorders. Mathieu Jaboulay performed the first sympathetic ablation for an ischaemic foot ulcer in 1898 by perivascular denudation [151]. René Leriche, in 1913, extended the use of this procedure [152]. In 1924, Royle [153] performed the first lumbar sympathectomy for spastic paralysis, whereas Diez [154] was the first to use this procedure for ischaemic lesions of the limbs. Adson [155] in 1925 extended the indications to include vasospastic disorders.

Ischaemia results from several obstructive and spastic disorders.

#### Obstructive ischaemia

Atherosclerosis and thromboangiitis obliterans (TAO also called Buerger's disease) are the main pathologies causing ischaemia, the former affecting primarily the leg, whereas the latter having a tendency to involve the hands as well in its advanced stages. Atherosclerosis may limit walking due to insufficient muscular oxygenation during exercise (intermittent claudication) or if more severe may cause tissue loss. Several studies which have elucidated the pathophysiological effect of sympathetic ablation on muscular perfusion [156–167] have shown that sympathectomy is not beneficial in intermittent claudication. Although rare publications still report on sympathectomies performed for atherosclerosis causing digital ulcerations [168], success is limited and far inferior to that for Raynaud's phenomenon The present state is that sympathectomy is not indicated in the treatment of atherosclerotic ischaemia.

TAO is a non-atherosclerotic segmental vasculitis affecting the small- and medium-sized arteries and veins of the extremities and is strongly associated with smoking [169, 170]. Upper limb sympathetic ablation has been successfully performed for intractable pain, ulceration or gangrene [171–174]. However, in a recent analysis of 344 cases, the duration of effect was limited, especially if smoking continued [175].

Whatever the source, microemboli may induce digital ischaemia and be unamenable to embolectomy. In such instances, sympathectomy may prove to be beneficial. Whatever the source of emboli [176–180], the treatment of all these lesions should be directed to the primary pathology, reserving additional sympathetic ablation for the cases in which digital ischaemia persists. A preliminary sympathetic chemical block may indicate likelihood of the successful sympathetic ablation [177].

## Vasoconstrictive ischaemia

Vasoconstrictive ischaemia may occur in a series of pathologies: primary Raynaud's phenomenon, scleroderma, rheumatoid arthritis, lupus erythematosus, paraneoplastic syndrome and vibration syndrome.

Raynaud's phenomenon is a paroxysmal arterial or arteriolar vasospastic disorder predominantly afflicting the fingers, characterized by digital ischaemia induced by cold or emotional stress [181]. Raynaud's phenomenon may be primary, or secondary to other underlying diseases (collagen diseases, paraneoplastic syndrome, frostbite and vibration syndrome). When present, treatment should be directed to the primary pathology, as well as prevention of cold exposure and medications such as vasodilator drugs and calcium channel blockers [181]. In advanced stages, when persistent ischaemia, ulceration and gangrene develop upper thoracic sympathectomy may alleviate ischaemic pain, maximize tissue preservation and limit amputation [182, 183]. However, the effect of sympathetic ablation was found to be temporary in the majority of cases [182, 183]. This was recently reconfirmed in a "summary of evidence" study [184]. Therefore, an initial attempt to obtain sympathetic block by phenol injections [185] may be beneficial, leaving the sympathetic chain intact for a repeated ablation for recurrent symptoms. Reoperative digital sympathectomy has been proven to be successful [186].

In scleroderma, half of all patients develop digital ischaemia. Initial treatment is medical, including prevention of exposure to cold, stress and trauma; smoking cessation, and oral medications like vasodilating agents, statins, endothelin receptor antagonists and phosphodiesterase-5 inhibitors [187]. If digital ulcers develop, intravenous prostacyclins may help [187]. Upper thoracic sympathetic ablation is occasionally performed for scleroderma with critical digital ischaemia [188, 189]. In the majority of reports for this indication, a periarterial [167] or digital [190, 191] approach is described. The reason is probably due to the additional surgical orthopaedic procedures required, which are performed by hand orthopaedic surgeons. The results are good on short term and may persist or deteriorate according to the progression of the basic disease [167]. There are no studies comparing digital versus upper thoracic sympathectomy. If an additional procedure in the hand is required, performing a local sympathectomy is logical. However, the perivascular digital approach requires an individual operation for each involved finger, whereas an upper thoracic sympathetic ablation affects all digits and, logically, should be the procedure of choice in cases with multiple affected fingers.

Digital ischaemia has been described in rheumatoid arthritis and lupus erythematosus (two collagen diseases), and sympathetic ablation has been reported to be beneficial [167]. One sign of the paraneoplastic syndrome is digital ischaemia. In one such reported case with severe bilateral Raynaud's phenomenon, bilateral sympathectomy permanently relieved ischaemia of the hands until demise of the patients after 10 months [192].

The first description of the pathophysiology of frostbite was given by Larrey, Surgeon-General of the imperial French armies, who participated in the 1812 disastrous retreat from Moscow of the Grande Armée [193]. Frostbite damage develops through three major mechanisms: direct cellular injury, hypoxia, and the release of vasoactive and toxic by-products [194]. The current literature contains work both discrediting [195] and supporting [196–198] the effect of sympathetic ablation in frostbite injuries. According to these studies, sympathetic ablation in the immediate post-thawing period may be detrimental by increasing oedema and accelerating tissue destruction [199]. However, if delayed until 24–48 h, the opposite effect has been observed. Pain and paraesthesia are also improved [200]. The beneficial effect of sympathectomy in the long term has been confirmed in a recent study [201].

Hand-arm vibration syndrome is one of the most common occupational disorders in the industrialized world [202]. Symptoms include paraesthesiae and pain, unrelated to episodes of "white fingers" [203]. In advanced cases, vasospasm and ischaemic changes including gangrenous lesions have been observed [202, 204]. However, unlike the case of other primary pathologies and Raynaud's phenomena, there is a striking paucity of studies advocating sympathetic ablation in the treatment of vibration-induced ischaemic lesions. Probably, this is because simply avoiding vibration improves symptoms [202].

#### Hypertension

The treatment of hypertension by sympathetic ablation was initiated in the 1930s [205], first by the transthoracic approach and later at the infradiaphragmatic level [206]. The efficacy of sympathetic ablation in the treatment of hypertension was confirmed in the study of Smithwick and Thompson [207] who in 1953 compared 1266 hypertensive patients following thoracolumbar sympathectomy with 467 hypertensive controls and observed 5-year mortality rates of 19 and 54 %, respectively. Of those who survived surgery, 45 % had significantly lower blood pressure afterwards, and the therapeutic effect of sympathectomy lasted 10 years or more. With the advent of modern effective antihypertensive drugs with minimal side effects, sympathectomy was largely abandoned in the 1960s [208]. However, there is a small percentage (but substantial number) of patients with resistant hypertension. For these patients, renal sympathectomy remains a useful treatment. Open periarterial stripping of the renal vessels was used in the past to obtain renal sympathetic denervation [209]. With the advent of endovascular procedures and the possibility to ablate the adventitia by intraluminal radiofrequency [210], renal sympathetic ablation became a relatively simple procedure and gained popularity. The long-term efficacy of the procedure remains to be determined. At present, it is not considered to be a routine procedure for resistant hypertension, a better design and future randomized studies being required [211]. The thoracic approach for sympathetic ablation to treat hypertension is obsolete.

#### **Psychiatric indications**

As odd as it may sound, sympathetic ablation for a psychiatric indication has been performed, not in the early years of surgery, but as late as this century [212]. In this article, the authors reviewed their experience with sympathetic ablation in the treatment of blushing, excessive sweating and "social phobia with and without physical symptoms". A social phobia or, as it should be better called, social withdrawal or anxiety may be secondary to a physical problem, like palmar hyperhidrosis or axillary overperspiration [213]. It has been shown that hyperhidrotics show higher stress levels in social interactions and more depressive symptoms compared to control subjects [214]. Social withdrawal may also be secondary to blushing [81, 215, 216]. In these cases, it is understandable that curing the underlining condition, patients' social withdrawal will also be reduced. The reverse, namely overperspiration, being secondary to social anxiety disorders is also possible [217]. However, treating a primary phobia by sympathetic surgery has no scientific basis in the literature.

A search in the Medline under the terms "Social Phobia and Sympathetic Ablation" has yielded only five publications dealing specifically with the subject, all by the same group of authors [218-222]. A scrupulous review of these publications leads to the following two conclusions. Firstly, the authors' classification is based on an hypothesis of neural pathways, but there is no objective proof for it being correct. Secondly, there is no objective proof that it is correct to use sympathetic ablation in the treatment of a primary phobia/anxiety. The fact that all treatments have failed is no justification to treat a primary phobia by sympathetic surgery [219, 221]. In their article [219], the authors claim to have operated upon 45 people for a social phobia and performed a follow-up on 20 patients. However, all they present in the article is a single case report! Performing sympathetic ablation for a primary social phobia remains equivalent to performing a scientifically yet unproven human experiment. There is no psychiatric indication for sympathetic surgery.

## Conclusions

Thoracic sympathetic ablation is currently the only curative modality for primary palmar hyperhidrosis. Although serious sequelae may ensue, patients with severe symptoms should be offered this possibility, provided they receive a detailed information regarding side effects. Presently, there are several effective non-surgical and surgical modalities of treating axillary hyperhidrosis. As the results of sympathectomy for axillary hyperhidrosis are inferior to those for palmar hyperhidrosis, sympathetic ablation should be reserved only for cases in which the operation is performed primarily for concomitant palmar hyperhidrosis. Sympathetic ablation should be reserved as the last line of treatment for facial overperspiration and blushing. Compensatory hyperhidrosis, the development of excessive sweating in areas of the body unaffected anatomically by the sympathetic denervation, and to a lesser degree gustatory sweating, are the major drawbacks of sympathetic surgery for primary hyperhidrosis, which requires its strictly judicious use, for these cases. Thoracic sympathetic ablation has a place in some rare and strictly selected cases of angina, arrhythmias and cardiomyopathy unresponsive to standard medication. Sympathetic ablation may be beneficial if performed in the early stages of complex regional pain syndrome, and some painful abdominal pathologies, in particular pancreatic or other malignancies. The use of sympathetic ablation for ischaemia has substantially declined, but still has a place in thromboangiitis obliterans and selected cases of microemboli, primary Raynaud's phenomenon, Raynaud's phenomenon secondary to collagen diseases, paraneoplastic syndrome and frostbite. In dubious cases, a preliminary chemical sympathetic block may suggest what benefit could be expected from the procedure. Since the advent of endovascular renal sympathetic ablation, thoracic sympathetic procedures for hypertension became obsolete. Sympathetic ablation is being used by a narrow group of surgeons for cases of primary phobias, but it should be emphasized that there is no scientific basis to perform sympathetic surgery for any psychiatric indication.

#### **Compliance with Ethical Standards**

**Disclosures** Moshe Hashmonai, Alan E. P. Cameron, Peter B. Licht, Chris Hensman and Christoph H. Schick have no conflicts of interest or financial ties to disclose.

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