Chapter 6
Management of Localized Low-Grade Follicular Lymphoma

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Overview of Localized Disease

Follicular lymphoma (FL) is the most common indolent non-Hodgkin lymphoma. The majority of FL cases are advanced stage at diagnosis, with frequent nodal and bone marrow involvement. Approximately 20% of patients have localized (stage I–II) disease at the time of presentation [1, 2]. Because early-stage FL is uncommon, it is important to exclude the presence of distant disease with a complete staging evaluation, including a bone marrow biopsy and PET-CT scan, before embarking on a course of definitive local therapy.

In patients diagnosed with localized FL, the median age is 60 years. These patients typically have a good performance status and normal LDH. Disease is often limited to one nodal region at a peripheral site, such as the neck or inguinal basin. Extranodal involvement is observed in approximately 25% of cases [3].

There is great variety in the management approaches used for early-stage FL. The National LymphoCare Study was a multicenter, longitudinal, observational study that included patients treated for FL in academic and community practices. It aimed to identify current demographics and patterns of care in the United States. Of the 2728 subjects enrolled, 474 patients had stage I disease at diagnosis. Management of these patients with stage I disease consisted of radiation therapy (RT) in 23%, rituximab alone in 13%, rituximab with chemotherapy in 30%, and observation in 29%. Among stage I patients not receiving RT as

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initial therapy, 21% received RT within 90 days of completing initial treatment, suggesting a planned combined modality approach [2]. Thus, various treatments are used frequently in this setting. Furthermore, all of these approaches have been associated with favorable outcomes [4]. As no clinical distinction is reliably made between grade 1 and 2 diseases and as many centers treat grade 3A or grade 3B disease as DLBCL, the goal of this chapter is to discuss the management strategies for early-stage grade 1–2 FL.

Radiation Therapy

Radiation therapy (RT) is a recommended approach for stage I or contiguous stage II, low-grade (grade 1–2) FL and has been the historical standard of care. Multiple institutions have reported their experience treating localized FL using definitive RT [5–9], as summarized in Table 6.1. These series demonstrated local control rates of >90% within the irradiated area. However, relapse with systemic disease outside of the radiation field was common, with 10-year relapse-free and overall survival rates of approximately 50% and 60%, respectively. A plateau in the disease-free survival curve was observed beyond 10–15 years, suggesting that a proportion of patients were cured with RT alone. An important limitation of these older series is that at least some patients were treated before metabolic imaging was used for staging. Therefore, patients may have had undiagnosed advanced-stage disease. Furthermore, the RT fields were more extensive and salvage options more limited, so it may be difficult to apply the data to today's experience and prognosis discussions.

To address these concerns regarding older series, the International Lymphoma Radiation Oncology Group (ILROG) reported the outcomes of curative RT for localized FL in patients treated in the modern era, all of whom were staged using PET-CT scans prior to RT. In this cohort, the 5-year freedom from progression (FFP) was 70.2% and overall survival was 95.8%. The 5-year FFP was 74.3% for the subset of patients with stage I disease [10]. Thus, outcomes after RT in these PET-staged patients were better than in some earlier series, suggesting that the curative potential of RT for truly localized FL may have been underestimated previously.

Radiation Dose

The accepted radiation dose for the treatment of FL was established by two randomized dose de-escalation studies. First, Lowry et al. randomized patients with indolent NHL, primarily grade 1–2 FL, to receive the historical, standard dose of 40–45 Gy or the experimental, reduced dose of 24 Gy. No difference in disease response, local progression, disease-free survival, or overall survival rates was observed between the

Table 6.1 Reports of definitive treatment of stage I/II follicular lymphoma with radiation therapy

Institution	Number of patients	Years of treatment	Median follow-up (years)	Freedom from relapse	Overall survival	Local control	Radiation dose	Radiation field	Comments
Princess Margaret Hospital [5]	190	1967–1978	10.6	53%, 12 years	58%, 12 years	87%, 12 years	20–48 Gy	IFRT	No difference in local control for doses between 20 and 40 Gy, when controlling for other prognostic factors
Stanford University [6]	177	1961–1994	7.7	44%, 10 years	64%, 10 years		35–50 Gy	TLI, STLI, EFRT, IFRT	Relapse was rare beyond 10 years after RT
University of Florida [7]	72	1965–1995	8.5	59%, 10 years	46%, 10 years	Four in-field recurrences	20–50 Gy	TLI, EFRT, IFRT	RT dose was not a significant prognostic factor on multivariate analysis, suggesting that low dose was adequate
Harvard University [8]	106	1972–2000	12	46%, 10 years	75%, 10 years	Seven in-field recurrences	Median 36.7 Gy	EFRT, IFRT	The leading cause of death was lymphoma. Second malignancy rates did not differ from the expected number, based on SEER data.
British Columbia Cancer Agency [9]	237	1986–2006	7.3	49%, 10 years	66%, 10 years	3 isolated in-field recurrences; 11 in-field and distant recurrences	20–40 Gy	EFRT, INRT ≤5 cm	No difference in patterns of failure or survival outcomes in patients treated with EFRT or INRT ≤5 cm. Relapse beyond 10 years after RT was rare
International Lymphoma Radiation Oncology Group [10]	310	2000–2016	4.2	70.2%, 5 years	95.8%, 5 years	Six in-field recurrences	Median 30 Gy (range 24–36 Gy)		All patients were staged by PET-CT prior to RT

arms. Lower toxicity rates were observed in the 24 Gy arm [11]. Since no loss of efficacy was associated with the reduced dose compared with the previous standard dose, 24 Gy in 12 fractions became the accepted dose for definitive RT.

The reported efficacy of even lower radiation doses prompted the FORT trial. This non-inferiority study randomized patients to receive a total dose of 24 Gy in 12 fractions or 4 Gy in 2 fractions. In the patients treated with just 4 Gy, the overall response rate (ORR) was 81% (48% complete response [CR] and 32% partial response [PR]). The CR rate was higher in patients treated with 24 Gy. However, given the high ORR, ease of administration, and minimal toxicity associated with 4 Gy, the authors concluded that this very low dose is a useful alternative to 24 Gy in instances when local control is less of a priority [12].

Additionally, 4 Gy should be considered if there is concern that 24 Gy may be associated with excess toxicity. As one example, in the treatment of FL of the orbit, 4 Gy in two fractions is associated with high response rates and minimal toxic effects [13, 14]. Conversely, moderate doses to the orbit, in the range of 24 Gy, have been associated with late toxicity in a substantial proportion of patients [15]. Therefore, a reasonable approach for FL of the orbit is to treat with 4 Gy initially and to escalate the dose only if needed for refractory disease. This strategy may be used in other settings, as well, based on the risk of toxicity from 24 Gy and the importance of establishing local control.

Radiation Volume

Historically, radiation field design has included total lymphoid, extended field, involved field, and involved site techniques. No randomized studies have compared larger and smaller fields. However, retrospective data published by Campbell et al. show no significant difference in the patterns of failure or survival outcomes in patients treated with large, regional fields or smaller fields encompassing the involved node(s) with margins of no more than 5 cm. The authors conclude that the field size may be reduced to include only the involved nodes with a margin of $\leq$5 cm, without loss of efficacy [9]. Based on such data, the ILROG guidelines recommend a “generous” involved site approach for the definitive treatment of FL [16], as shown in Fig. 6.1.

Systemic and Combined Modality Therapy

Lymphoma remains a common cause of death, and distant relapse is the dominant pattern of failure after initial treatment with RT for limited-stage FL. The use of

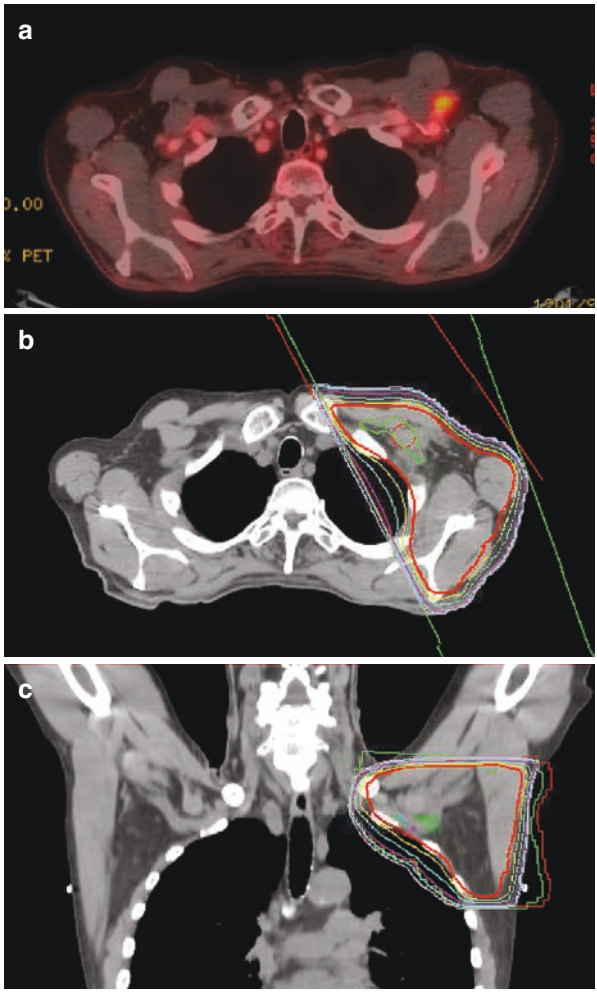

Fig. 6.1 A 67-year-old male presented with a left axillary mass. An excisional biopsy revealed grade 2 follicular lymphoma. A PET-CT showed a 3.7 cm left axillary lymph node with an SUV of 4, with no other evidence of disease (**a**). A bone marrow biopsy was negative for lymphomatous involvement. The patient was treated with definitive radiation therapy to a total dose of 24 Gy (axial slice in (**b**) and coronal slice in (**c**); red isodose line = 24 Gy)

systemic therapy, including cytotoxic chemotherapy, immunochemotherapy, and anti-CD20 antibody monotherapy, in combination with RT or alone, has been investigated by multiple groups attempting to address these issues. Thus far, while improvements in PFS have been seen with some regimens/combinations, no reproducible benefit in OS has been demonstrated, as summarized in Table 6.2. Thus, the use of systemic therapy in limited-stage FL is not recommended routinely outside a trial or in select cases with high burden disease.

Table 6.2 Reports of chemotherapy or combined systemic and radiation therapy for limited-stage follicular lymphoma

Institution	Number of patients treated with systemic therapy	Treatment regimen (s)	Years of treatment	Median follow-up (years)	Freedom from relapse	Overall survival	Comments
Prospective							
MD Anderson [17]	85	30–40 Gy IFRT + cytotoxic regimen without Rituxan	1984–1992	10	72% at 10 years	80% at 10 years	Myelodysplasia and second cancer rates were worrisome
MSKCC [18]	44	RT (regional median 40 Gy) +/− CHOPx6	1980–1988	7	83% vs. 47% $p < 0.03$	88% vs. 66% NS	
British National Lymphoma Investigation [19]	148	RT (25–35 Gy) +/− oral chlorambucil	1974–1981	18	33% vs. 42% at 10 years NS	52% vs. 42% at 10 years NS	
Retrospective							
Ruella et al. [20]	43	Rituximab ×4 cycles → RT	1999–2011	8.6	51% at 10 years	84% at 10 years	NS difference in PFS or OS vs. RT alone on MVA
LymphoCare [4]	206	CT and RT or rituximab alone	2004–2007	4.75	Not reported	Not reported	MVA showed PFS benefit but not OS benefit for immunochemotherapy +/− RT vs. RT alone or observation

Janikova et al. [21]	28	Rituximab or rituximab-RT	1999–2012	<5	85.7–91.7% at 3 years	85.7–100% at 3 years	Small retrospective; limited follow-up in Rituxan arms in particular
Michallet, et al. [22]	87	Rituximab, rituximab + CT, +/− RT	1967–2011	7	At 7.5 years, 60% for rituximab + CT vs. 19–26% for other therapies	66–100% at 7.5 years; NS difference between cohorts	Poor outcomes for RT alone and observation cohorts attributed to imbalance in referral pattern; limits interpretation
Mondello et al. [23]	72	Rituximab +/− IFRT	1995–2012	8	Median 5 years rituximab, 6 years rituximab + RT	Not specified	Improved PFS vs. RT but NS difference in OS
Oslo University [24]	139	CT with or without RT	1980–2005	15	At 10 years, ~25% for CT, ~45% for observation, ~55–60% for RT or CT + RT	At 10 years, ~50% for CT or observation, ~70% for RT or CT + RT	Follow-up shorter for systemic therapy-treated patients but not specified; few rituximab patients. NS difference on MVA between treatment groups
Sancho et al. [25]	73	CT with or without RT	1989–2012	6.8	At 10 years, 61% for CT + RT and 39% for CT	At 10 years, 81% for CT + RT and 72% for CT	NS difference in outcomes on MVA between treatment groups; ~1/2 patients received rituximab

IFRT involved field radiation therapy, *CHOP* cyclophosphamide, doxorubicin, vincristine, prednisone, *RT* radiation therapy, *CT* chemotherapy, *NS* not significant, *PFS* progression-free survival, *OS* overall survival

Historical Trials of Adjuvant Chemotherapy with Radiotherapy

Early investigations of adding systemic therapy to RT in FL occurred in an era before "rigorous" staging techniques or modern classification of indolent NHL, which complicates their comparison to current series. Overall, they demonstrated that systemic therapy conferred no OS benefit and added toxicities not considered justifiable for treatment of asymptomatic, low-burden disease.

- Seymour et al. [17] at MD Anderson Cancer Center conducted a prospective study of risk-adapted chemotherapy (cyclophosphamide, vincristine, prednisone, bleomycin +/− doxorubicin depending on risk features) with 30–40 Gy IFRT in indolent NHL including 85 patients with limited-stage FL from 1984 to 1992. With a median follow-up of 10 years, 10-year PFS was 72% and OS 80% in FL patients. However, two cases of myelodysplasia and ten second malignancies (four within RT field) and the acute toxicities of therapy tempered enthusiasm for this regimen, without direct comparative proof of its benefit in comparison to RT alone.
- Yahalom et al. [18] at Memorial Sloan Kettering Cancer Center conducted a randomized prospective trial of regional RT followed by six cycles of CHOP chemotherapy in 44 patients with stage I intermediate-low-grade NHL between 1980 and 1988. At a median follow-up of 7 years, there was an improvement with combined modality therapy for PFS (83% vs. 47%) but no significant difference in OS (88% vs. 66%, $p = 0.2$). Of note, these patients' treatment predated the use of advanced imaging techniques and the current classification of NHL.
- The British National Lymphoma Investigation group conducted a randomized trial [19] of low-grade limited-stage NHL from 1974 to 1981 in 148 patients, who received either RT alone or RT and oral chlorambucil. At a median 18-year follow-up, no PFS or OS difference was seen.

Retrospective Comparisons of Radiation Alone to Systemic Therapy with or Without Radiation

More contemporary retrospective studies have evaluated varying combinations of the anti-CD20 antibody with systemic therapy regimens and/or RT. These have found at most a suggestion of benefit for PFS but not OS with the addition of systemic therapy to RT:

- Ruella et al. [20] evaluated patients with limited-stage grade 1–3A FL who underwent either RT alone ($n = 51$) or RT followed by four cycles of rituximab anti-CD20 therapy ($n = 43$). At a median follow-up of 10.9 years, they found improved 10-year PFS in the combined therapy vs. RT alone group on univariate

analysis, but not on bivariate analysis adjusting for stage. No difference in OS was seen.

- The LymphoCare [4] observational study included a subset report of stage I patients who were staged with CT or PET and bone marrow biopsy. This analysis included a comparison of 206 patients treated with systemic therapy and RT to those managed with observation, anti-CD20 therapy, immunochemotherapy, or RT alone. A PFS benefit over RT alone or observation was seen on multivariable analysis for those receiving either immunochemotherapy or combination systemic therapy with RT. Again, no OS difference was identified. No difference was seen in PFS for these combinations vs. anti-CD20 monotherapy.
- Janikova et al. [21] reported a small retrospective series with short follow-up (5 years or less for all subgroups) in which 93 patients with stage I–II grade 1–3A FL were treated with RT alone ($n = 65$), rituximab alone ($n = 14$), or rituximab and RT ($n = 14$). The 3-year PFS was worse for RT alone vs. rituximab/RT or rituximab alone (57.4% vs. 85.7% vs. 91.7%, respectively). However, no multivariable analysis was performed, and time periods and follow-up were substantially different between the RT and combination/rituximab arms. OS was not significantly different.
- Michallet et al. [22] reported a series of 145 early-stage FL patients undergoing RT, rituximab, chemotherapy, chemotherapy and rituximab, chemotherapy and RT, or observation. Improved 7.5-year PFS was seen in the immunochemotherapy arm (60%) compared to all other arms (19–26%). However, the exceptionally poor performance of these other arms, especially RT, compared to multiple other series was noted and ascribed by the authors to referral of patients to their center at the time of relapse. Notwithstanding this issue, which clouds our assessment of the study comparison, OS was not significantly different between arms.
- Mondello et al. [23] reported on 108 early-stage FL patients treated with RT ($n = 36$), rituximab ($n = 38$), or combination rituximab and RT ($n = 34$) with 8 years of follow-up. Despite the higher incidence of adverse features in the rituximab-containing groups, they observed improved PFS for rituximab alone or in combination with RT, compared to RT alone (median PFS of 5–6 years vs. 2.3 years). While OS trended toward improvement in the rituximab arms ($p = 0.059$), it did not reach significance.
- The Oslo University Hospital series [24] included 404 early-stage FL patients who underwent RT, observation, chemotherapy, or chemotherapy and RT. Most patients were treated before the introduction of rituximab. On multivariate analysis, no differences in PFS or OS were seen according to initial management.
- Sancho et al. [25] reported on 130 patients with limited-stage FL managed with RT ($n = 46$), RT and chemotherapy ($n = 30$), chemotherapy alone ($n = 43$), or observation ($n = 11$). No OS benefit was seen, but in those treated with combined RT and chemotherapy, multivariable analysis indicated significantly improved PFS (HR 0.3, $p = 0.024$).

Ongoing Trials

- MD Anderson Cancer Center is conducting a trial of RT with rituximab followed by maintenance rituximab (NCT0143628).
- The German Low-Grade Lymphoma Study Group (GLSG) is conducting the MIR (Mabthera® and Involved field Radiation) phase II trial of induction rituximab followed by restaging and concurrent rituximab with RT (NCT00509184).

Observation

Despite the data for potentially curative treatment with RT, some have argued against its use in limited-stage disease, due to the long, indolent natural history of FL [26], the frequent relapses outside radiation fields, and the lack of improvement in OS. Instead, they have argued for observation in the setting of low-volume disease. A desire to avoid or delay the toxicity of immediate treatment has thus extended to the limited-stage population. This practice pattern is evident from the significant rate of observation, in lieu of immediate treatment, in large registry studies, with over 400 limited-stage FL patients each, conducted in the United States (28.7%) [2] and Norway (~15%) [24]. While published series of selected patients undergoing observation have demonstrated no difference in OS compared to immediate therapy (excepting a SEER analysis comparing RT- to non-RT-treated patients, which did not delineate observed vs. systemic therapy-treated patients [27]), only limited data are available regarding observation in the setting of limited-stage disease. Nonetheless, observation may be the preferred option in patients with significant co-morbidities, noncontiguous stage II disease, or fully resected stage I disease.

Observation Outcomes

Data for observation in limited-stage low-grade FL stems primarily from retrospective studies with varying time periods, staging methods, definitions of observation, and reasons for treatment initiation. A particularly rigorous investigation from Stanford evaluated 43 patients with a median follow-up of 86 months, who underwent uniform staging with bone marrow biopsy and computed tomography. Of note, this study was conducted in the pre-PET era. These patients did not receive any therapy for at least 3 months after diagnosis. They achieved an impressive median overall survival of 19 years and 10-year freedom-from-treatment rate of 56%. These outcomes were superior to those from a series of patients treated with RT [6] from the same institution (median overall survival of 13.8 years). However, for the 37% of patients who required treatment, overall survival was 8.3 years. Furthermore, four patients experienced transformation, even in this highly selected population.

Soubeyran et al. [28] reported on 26 patients at their institution who were followed with observation after full excision of their disease ("stage I0"). They reported a 50% crude rate of freedom from relapse after a median follow-up of 6.3 years. The predominant pattern of relapse was at distant sites.

In another single institutional retrospective series, Michallet et al. [22] observed 36 patients (definition not given in manuscript) with unclear median follow-up (likely short given the overall cohort was 7-year median follow-up and most observation patients were treated in more recent era). At 7.5 years, the progression-free survival rate was 26% and overall survival was 72%.

Further data has been made available from registry studies or investigations of observation in all stages of disease, though not all have specified outcomes for the limited-stage cohort [29, 30]. The LymphoCare prospective observational registry of FL patients managed from 2004 to 2007 at community practices primarily reported outcomes for stage I disease that was "rigorously" staged by bone marrow biopsy and either CT or PET. Thirty-five patients were managed with observation, defined as having received no therapy for 3 months after diagnosis [4]. This cohort did not have actuarial outcomes specified; however, OS was reported to be not significantly different for patients who were observed or given immediate therapy, with a median follow-up time of 57 months. Lastly, a recent series from the Oslo University Hospital [24] compiled outcomes of 63 patients undergoing observation. With a median follow-up of 15 years, the crude rate of progression was 46%, and no difference in OS was observed for patients who were observed compared to those who received immediate therapy.

Selection for Observation

As observation is used for differing reasons, selection criteria in published work have varied. Common reasons include the following:

- Fully excised stage I FL.
  - *Rationale*: Lower benefit to local therapy in the absence of gross disease.
  - *Data*: Soubeyran et al. [28] reported a series of 26 patients achieving 50% crude relapse-free survival at 6.3 years of follow-up. In the Oslo University Hospital series [24], those patients undergoing observation after full excision demonstrated superior PFS compared to those with asymptomatic residual disease ($p = 0.03$).
  - *Comment*: In rigorously staged patients with no residual disease after excisional biopsy, observation may be considered after counseling patients that a substantial progression risk may remain. Given the low morbidity of modern doses of radiation for FL, performing a more radical surgery to allow observation is not supported.

- Concern over RT toxicity due to large field requirement and/or location of disease.
  - *Rationale*: Multifocal areas of noncontiguous FL may require large fields to encompass all sites of disease, resulting in more treatment-related toxicity. Furthermore, noncontiguous stage II disease may portend a higher risk of occult distant involvement outside of the RT field. Additionally, observation might be recommended if disease is in close proximity to radiosensitive normal tissues, causing concern for RT-induced toxicity. Together, a lower therapeutic ratio from local RT may justify observation.
  - *Data:* In the Stanford series [31], the rationale for observation in 33% of cases was large abdominal field/salivary gland involvement. Most patients (74%) had stage II disease. In the Oslo series [24], observation was recommended in 43% of cases based on stage II presentation with nonadjacent nodal involvement.
  - *Comment*: As noted in the previous RT section, randomized controlled trials of RT for indolent B-cell NHL have recently established a relatively low dose of 24 Gy as the standard dose, 4 Gy as an alternative dose with lower control but minimal toxicity, and smaller fields for treatment. Thus, while select cases of discontinuous widespread or bulky stage II disease may merit consideration of management as "advanced" disease with observation [32], an attractive alternative is treatment with RT to just 4 Gy. This very low dose results in high response rates with minimal risk of toxicity.
- Patient comorbidities.
  - *Data:* No specific data.
  - *Comment:* As with other malignancies, an understanding of the life expectancy of a sick or elderly patient relative to the natural history of limited-stage FL should guide management. In the setting of a limited life expectancy, the use of either observation or very low-dose (4 Gy in two fractions) RT may be appropriate.

Comparison to Treatment

Comparison of outcomes after observation vs. immediate treatment is challenging. First, observation cohorts are subject to selection bias. Furthermore, most data for observation remains retrospective, with follow-up shorter than the ~10 years typically needed before the PFS curves plateau after RT. With that said, currently published series of observation for limited-stage low-grade FL have not demonstrated significant differences in OS compared to immediate therapy with varying approaches, including RT, combined modality systemic therapy, and radiation and anti-CD20 therapy combinations. These comparative data are summarized below:

- The Oslo University Hospital [24] analyzed 404 patients with early-stage FL managed with either observation (15%; fully excised stage I or discontinuous stage II), RT alone (48%), systemic therapy (16%; including cytotoxic regimens, immunochemotherapy, or anti-CD20 antibody alone), or combined chemotherapy and RT (16%). On univariate analysis, RT-treated patients demonstrated improved OS compared to systemic therapy-treated patients and a trend toward improved OS compared to observation patients ($p = 0.054$). However, multivariable analysis demonstrated no difference in PFS or OS between cohorts.
- Michallet et al. [22] evaluated 145 patients with limited-stage FL treated or referred upon relapse to their hospital from 1967 to 2011 with a median 7-year follow-up. Treatment was observation ($n = 36$), RT ($n = 21$), rituximab alone ($n = 7$), chemotherapy/RT ($n = 18$), or immunochemotherapy ($n = 36$). Monotherapy with rituximab was associated with a poor complete response rate. Only immunochemotherapy was associated significantly with improved PFS but no difference in OS. The authors conclude that observation is reasonable, but, when treatment is required, immunochemotherapy may be preferred. However, this conclusion is challenged by an exceptionally poor performance in 7.5-year PFS of their observation (26%), RT (19%), chemotherapy/RT (26%), and chemotherapy (23%) cohorts. These PFS rates are significantly inferior to outcomes reported for each approach in multiple other series. The authors suggest that these outcomes were poor, because some patients were referred to their center at the time of relapse.
- The LymphoCare [4] observational registry evaluated a cohort of 206 patients with stage I FL who underwent "rigorous" staging, including a bone marrow biopsy and PET or CT. The subgroup of 35 patients who were observed experienced no significant difference in OS compared to those treated initially with immunochemotherapy, anti-CD20 therapy alone, RT alone, or combined chemotherapy and RT. However, PFS was superior for those receiving either combined RT and systemic therapy or immunochemotherapy.

Conclusion

A variety of management approaches are used for early-stage, low-grade FL. The standard of care for stage I and contiguous stage II disease remains involved site RT. Typically, a dose of 24 Gy is used for definitive therapy; however, a total dose of just 4 Gy is reasonable in some cases. Incorporation of systemic therapy into management may result in improved PFS, but no improvement in OS has been shown. This strategy is an area of active study. Lastly, observation may be an appropriate strategy in select patients. A long natural history and evolving treatment approaches complicate the study of FL. Multi-institutional collaboration, with standardized pretreatment evaluations, management strategies, and follow-up schedules, is recommended to provide further insight into the optimal treatment of early-stage grade 1–2 FL.

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