

Lymphoma Network of New Zealand



Guidelines for the follow-up of patients in complete remission following treatment for Hodgkin Lymphoma

Introduction:

Evidence to guide development of Hodgkin Lymphoma follow-up protocols is sub-optimal with a very limited numbers of randomised studies available for analysis. Retrospective studies, non randomised prospective series, and review of various international consensus panel protocols have been studied in the development of these guidelines, which have been ratified by the New Zealand Lymphoma Network.

These guidelines are intended to provide a template for the assessment and monitoring of patients who have completed initial therapy for Hodgkin Lymphoma and achieved a complete response. They recommend minimum requirements for follow-up and it is recognised that in certain situations clinicians may opt for a more aggressive follow up strategy.

In the initial years following treatment completion, the focus of follow-up is detection of disease relapse. 10-20% of patients with early stage disease, and up to 40% of patients with advanced stage disease will relapse. Most relapses will have occurred within the first 5 years of follow up; however it must be noted that recurrent disease remains the leading cause of death in patients with Hodgkin Lymphoma for up to 15 years post diagnosis {1-5}.

At 5 years following treatment monitoring for late toxicities becomes a priority. The risks of various late effects depend on the age of the patient during treatment, gender, intensity and duration of therapy, the site and field of radiation, and patient co-morbidity and lifestyle factors. These guidelines include recommendations for long-term monitoring and a template letter to General Practitioners. Ideally individualised survivorship plans and clear advice for long term monitoring should be available for patients and General Practitioners when patients are discharged from specialist care.

1. Specialist Clinic Review:

A suggested schedule of patient contacts following completion of therapy:

- 2-3 monthly for 6 months
- 3-6 monthly from 6-24 months

- 6 -12 monthly years 3-5
- Consider discharge at 5 years in remission
- Alternate appointments with trained specialist nurses are acceptable. From 24 months post treatment until discharge a minimum annual clinic appointment is recommended with additional patient contact by phone or video conference etc.

Comments: Several studies concur- patient reported symptoms are the most frequent first indicator of disease relapse accounting for 55-81% of relapse presentation/detection. The detection of new lymphadenopathy, followed by development of B symptoms are the most frequently cited relapse symptoms. The vast majority of these symptoms occur between clinic appointments with only 11-14% of patient relapses detected on examination in clinic {2-4}. As will be detailed in later sections of these guidelines, imaging studies and laboratory tests alone are of even less value in the detection of relapse. These findings highlight the need for comprehensive patient education, the importance of early symptom reporting as well as a requirement for a flexible clinic service accommodating an urgent review policy.

In 2010 Dr B. Baker undertook a survey of New Zealand haematologists who were questioned regarding what they felt to be acceptable practice in the follow up of lymphoma- 48% of respondents felt that patient review by a specialist nurse at some follow up appointments was acceptable and 41% of respondents were comfortable with alternating clinic appointments and telephone interviews. In areas where travel to clinics is more challenging video conferencing or phone interview may be more acceptable to patients.

2. Laboratory testing.

Suggested schedule of laboratory testing after completion of therapy:

- FBC, ESR each visit or minimum of 6 monthly for 2 years

From year 2, continuing indefinitely:

- Minimum annual FBC
- Annual TSH if neck irradiated
- Annual lipid studies if cardiac irradiation, high dose chemotherapy or other CV risk factors.

Consider depending on patient:

- Iron studies pre discharge
- Annual sex hormones
- Annual renal function/electrolytes/LFT.

Comment: There is little evidence to determine the effectiveness of routine blood tests in the detection of relapsing Hodgkin Lymphoma. The ESR has been the sole abnormality at relapse in between 1-9% of patients in various case series {1,2,4}.

Bloods from 2 years on include monitoring for late effects and may vary depending factors including intensity of therapy, radiation fields, transfusion requirements and patient age.

3. Imaging.

- There is no requirement for routine surveillance imaging in patients who have documented Complete Response at the end of treatment.
- Surveillance CXR in patients who have had mediastinal disease is optional. Annual CXR in patients who have had thoracic radiation is advised.
- It is advised that CT or PET/CT scanning be reserved for the development of concerning symptoms, signs or laboratory abnormalities.
- Mammography should be performed annually in women who have received thoracic irradiation starting 8 years following radiotherapy or at age 40 years- whichever is sooner. Breast MRI should be considered as an alternative to mammography in younger women.

Comment: In case series CXR abnormality on routine screening was the first indicator of disease relapse in 5-23% of patients {1,2, 4}. The NZ lymphoma network working group did not feel that routine surveillance CXR should be specifically recommended in these follow up guidelines; however this practice is not actively discouraged either. In patients who have received mediastinal radiation an annual CXR is advised to monitor for late effects.

Regular surveillance CT or PET scanning of asymptomatic patients, known to be in complete remission following treatment is discouraged. Regular CT scanning may detect up to 9% of otherwise asymptomatic relapses in case series {1-5}; however several studies suggest routine CT surveillance is not cost effective and the overall diagnostic yield per CT scan is low {4,6-8,13,15}. In addition the toxicity of cumulative radiation exposure during years of surveillance imaging must be considered {10-12}.

4-6 monthly PET scanning may detect asymptomatic relapse in up to 14% of patients; however this percentage is likely to be lower in patients who had a documented negative PET scan at treatment completion. In addition almost 50% of PET scans performed during surveillance are subsequently found to be false positives, causing increased patient anxiety and unnecessary further

investigation/repeat scan {3,16,17}. PET scan surveillance does not appear to be cost effective {5,17}.

There is no evidence that detection of symptomatic versus asymptomatic relapsed Hodgkin lymphoma changes response to salvage chemotherapy or overall survival.

4. Survivorship, discharge from specialist clinic, and long term monitoring for late effects

- Discharge from specialist clinic should be considered after 5 years of sustained remission
- At the time of discharge from specialist clinic an individualised survivorship plan or letter summarising the patients' diagnosis, treatment received, significant complications during
- therapy, possible future health problems and instructions for ongoing care be given to the patient and the patients General Practitioner
- Patient education reiterating relapse symptoms, possible late effects and importance of life style factors which will ameliorate risk of future cancer, cardiac damage etc should be emphasised- e.g. avoidance of smoking, reduce sun exposure, maintaining healthy weight/diet...
- Patients should be seen and examined at least annually in primary practice with focus on cardiac and respiratory health, cancer risk/surveillance, endocrine/fertility function, osteoporosis prevention/screening, psychosocial and cognitive late effects.
- Skin within radiation fields should be examined at least annually.
- Colon cancer screening should begin 10 years earlier than general population.
- Unless otherwise stated participation in routine population based cancer screening as per NZ guidelines should be strongly encouraged. See imaging section for specific recommendation regarding breast cancer screening in women who have undergone mediastinal radiotherapy.
- Echocardiogram should be considered at end of treatment, then at 10 years post treatment in patients who have received $>200\text{mg/m}^2$ of anthracycline or cardiac irradiation. Early referral to a cardiologist is advised if any abnormality detected.
- The following vaccinations are recommended following therapy: annual influenza vaccination in all patients. If hyposplenic - 5 yearly pneumococcal, meningococcal, and HIB vaccinations also required and medical alert bracelet should be considered.

- End of treatment Lung function testing should be considered. Prior to discharge patients should be reminded of the risk of high oxygen concentrations following bleomycin and medical alert bracelet could be considered. In patients who have received carbamustine the risk of late pneumonitis should be explained.
- Irradiated blood product ????
- Patients are advised to attend annual dental review- especially if the head/neck has been irradiated.
- See laboratory testing for recommendations on ongoing blood testing post specialist clinic discharge.

Comment: Relapsed disease remains the most common of mortality in patients treated for Hodgkins lymphoma out until 14 years from diagnosis. Patients should be reminded of relapse symptoms and the importance of seeking early medical attention should they occur.

The risk of late effects following lymphoma treatment depend on a number of factors including sex, patients age at the time of therapy, intensity and type of treatment received, radiation fields, co-morbidity, and duration since therapy; therefore an individualised patient education and survivorship plan is ideal for patients being discharged from clinic. Many patients may move from their original treatment centre and it is important patients understand they will need indefinite monitoring- usually in a primary practice setting.

Appendix 1 contains an example of a Survivorship plan currently in use at Middlemore Hospital.

Appendix 2 contains an adaptable template patient discharge letter to GPs.

Resources detailing specific risks of late treatment effects are included in the reference section of these guidelines further information {5,6,9,20-}.

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Lymphoma Survivorship Care Plan

| Patient details | |
|-------------------|--|
| Patient name | |
| Patient NHI | |
| Date of Birth | |
| Date of diagnoses | |

| Professional Care Team | |
|---------------------------|--|
| Haematologist | |
| Clinical Nurse Specialist | |
| Cancer coordinator | |
| Social Worker | |
| General Practitioner | |

| Summary of disease at Diagnosis | | | |
|---------------------------------|------|------------------|--|
| Diagnoses | | | |
| • | | | |
| Study | Date | Findings/Details | |
| BMB | | | |
| CT scan | | | |
| Other: | | | |
| | | | |
| LDH | | ECHO | |
| Heb B | | HIV | |
| Extra Nodal sites: | | | |
| | | | |
| Stage : | | | |

| | | | | |
|--------------------|---------------------------------|----------------------------|----------------------------|---------------------------------|
| Prognostic score : | <input type="checkbox"/> 0 or 1 | <input type="checkbox"/> 2 | <input type="checkbox"/> 3 | <input type="checkbox"/> 4 or 5 |
|--------------------|---------------------------------|----------------------------|----------------------------|---------------------------------|

| Summary of Treatment | | | |
|---|--|--|--|
| Height: | | Pre-treatment weight: | |
| Post treatment weight: | | Pre-treatment BSA: | |
| Treated on clinical trial : | | | |
| - | | | |
| ECOG performance status prior to treatment: <input type="checkbox"/> 0 <input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4 | | ECOG performance status after treatment: <input type="checkbox"/> 0 <input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4 | |
| Chemotherapy protocol: <ul style="list-style-type: none"> • Nil required. | | | |
| Radiotherapy Site: Dose: | | Radiotherapy start date: Radiotherapy end date: | |
| Toxicities: | | | |

| Summary of Response | |
|--|--|
| CT Scan | |
| Bone marrow | |
| Other: | |
| Follow-up | |
| <p>We continued to see patient in clinic for 5 (five) years after diagnosis, initially every three months for two years and then 6 monthly for three years. We have now discharged you to your GPs care.</p> | |

| Long Term Care Planning | | | |
|--|---|---|---|
| <p>Potential late effects of disease, chemotherapy regimes and/or radiotherapy. Tick box if applicable to patient</p> <table style="width: 100%; border: none;"> <tr> <td style="width: 50%; vertical-align: top;"> <input type="checkbox"/> Cataracts <input type="checkbox"/> Hypothyroidism <input type="checkbox"/> Heart failure <input type="checkbox"/> Lung problems <input type="checkbox"/> Liver disease </td> <td style="width: 50%; vertical-align: top;"> <input type="checkbox"/> Kidney impairment <input type="checkbox"/> Increased risk of other cancers <input type="checkbox"/> Early menopause <input type="checkbox"/> Osteoporosis <input type="checkbox"/> Fatigue </td> </tr> </table> <p><u>Comments:</u></p> <ul style="list-style-type: none"> • | | <input type="checkbox"/> Cataracts <input type="checkbox"/> Hypothyroidism <input type="checkbox"/> Heart failure <input type="checkbox"/> Lung problems <input type="checkbox"/> Liver disease | <input type="checkbox"/> Kidney impairment <input type="checkbox"/> Increased risk of other cancers <input type="checkbox"/> Early menopause <input type="checkbox"/> Osteoporosis <input type="checkbox"/> Fatigue |
| <input type="checkbox"/> Cataracts <input type="checkbox"/> Hypothyroidism <input type="checkbox"/> Heart failure <input type="checkbox"/> Lung problems <input type="checkbox"/> Liver disease | <input type="checkbox"/> Kidney impairment <input type="checkbox"/> Increased risk of other cancers <input type="checkbox"/> Early menopause <input type="checkbox"/> Osteoporosis <input type="checkbox"/> Fatigue | | |
| <p>Call your GP if you have any of these symptoms:</p> <ul style="list-style-type: none"> • Palpable lymph nodes (lumps) • Night sweats/fever • Unexplained weight loss • Unexplained general un wellness | | | |
| Completed by: | Date: | | |
| Contact Details: | | | |

Appendix 2: Template letter for discharge of patient from specialist care to GP.

Dear Doctor.

Your patient was diagnosed with stage *(insert)* Hodgkin lymphoma in *(insert date)* and treated with *(insert)*. The patient has now been in remission for 5 years since completion on therapy and is well enough to be discharged from specialist clinic.

Although this patient should be urgently re-referred in the event of recurrent B symptoms or adenopathy, the risk of disease relapse is now very modest. Survivors of lymphoma do require lifelong follow up in primary practice is to monitor for the development of late treatment related toxicities including an increased risk of secondary malignancies, cardiac failure, ischaemic heart disease, endocrine dysfunction, respiratory illnesses and depression.

It would be appreciated if you would review this patient at least annually for a comprehensive assessment focusing on skin, cardiac, respiratory, endocrine (thyroid, bone, fertility) and basic psychosocial and cognitive function. As a lifelong precaution to prevent lung injury following bleomycin, your patient has been advised to avoid exposure to high oxygen concentrations (e.g. scuba diving, advise anaesthetist pre operatively).

Ongoing laboratory testing, imaging and treatment advised for your patient includes: *(delete as appropriate)*

- Annual full blood count, thyroid function testing, lipid profile, creatinine, liver function and testosterone *(FSH, LH)*
- Annual CXR
- Annual Mammogram starting at age *(insert date)*
- Echocardiogram at 10 years post treatment *(insert date)*
- Annual influenza vaccination
- 5 yearly pneumococcal, Hemophilus influenza and meningococcal vaccinations *(delete unless hypospemic)*
- Participation in all national cancer screening programmes. Screening for colon cancer should begin 10 year earlier than standard recommendations.
- Aggressive management of cardiac risk factors including hypertension, hyperlipidaemia, obesity etc. Early referral to a cardiologist is advised in the event of concerning signs or symptoms.
- Annual dental review has been recommended

Thank you for your ongoing care of this patient. Please contact us if you have any questions or concerns.