ANZUP
Cancer Trials Group Limited

These surveillance recommendations have been developed by a working group of ANZUP's Germ Cell Subcommittee and are provided for use within Australia and New Zealand. They are provided as recommendations only; clinicians should take into account individual circumstances and adaptations may be appropriate. These recommendations do not apply following adjuvant radiotherapy. Neither ANZUP nor the Germ Cell Subcommittee shall be liable for any inaccuracies, or adverse outcomes that may occur as a consequence of following these recommendations.

ANZUP STAGE I TESTICULAR CANCER SURVEILLANCE RECOMMENDATIONS					
Seminoma, No adjuvant therapy					
Year	Physical Examination (month)	Tumour Marker (month) +	CT Abdo/Pelvis (month)**	CXR (month)	Testosterone Assessment (month)
1	6, 12	6, 12	6, 12	-	6
2	18, 24	18, 24	18, 24	-	24
3	36	36	36	-	
4	48	48	-	-	
5	60	60	60	-	60
5-10	Some clinicians recommend follow up beyond 5 years. See below for discussion				
Seminoma, Post adjuvant carboplatin					
Year	Physical Examination (month)	Tumour Marker (month)	CT Abdo/Pelvis (month)	CXR (month)	Testosterone Assessment (month)
1	6, 12	6, 12	12	-	6
2	18, 24	18, 24	24	-	24
3	36	36	36	-	
4	48	48			
5	60	60	60	-	60
5-10	Some clinicians recommend follow up beyond 5 years. See below for discussion				
Non Seminoma, No adjuvant therapy					
Year	Physical Examination (month)	Tumour Marker (month)	CT Abdo/Pelvis (month)	CXR (month)	Testosterone Assessment (month)
1	1, 2, 3*, 4, 5*, 6, 8, 10, 12	1, 2, 3*, 4, 5*, 6, 8, 10, 12	4, 8, 12	4, 8, 12	6
2	15, 18, 21, 24	15, 18, 21, 24	18, 24	18, 24	24
3	30, 36	30, 36	36	36	
4	42, 48	42, 48			
5	60	60	60	60	60
Non Seminoma, Post adjuvant BEP chemotherapy					
Year	Physical Examination (month)	Tumour Marker (month)	CT Abdo/Pelvis (month)	CXR (month)	Testosterone Assessment (month)
1	6, 12	6, 12	6, 12	6, 12	6
2	18, 24	18, 24	18, 24	18, 24	24
3	36	36	36	36	
4	48	48			
5	60	60	60	60	60

*In the presence of lympho-vascular invasion
+ Option to reduce frequency of tumor marker assessment to coincide with routine testing of testosterone levels given reduced utility of serum tumor biomarkers in detecting seminoma recurrence[1]
**Consider MRI as an alternative to CT for abdominal imaging; AND/OR reduced frequency of abdominal imaging (see below text); AND/OR omission of concurrent pelvic imaging

Stage I Seminoma

A CT chest should be performed at baseline to exclude higher stage disease. Future imaging of the chest with either CXR or CT chest has not been shown to identify any unique recurrences of seminoma in numerous series, and is not recommended routinely[2].
The tumour markers to follow are BHCG and AFP. LDH does not add any value. These will uniquely detect approximately 3% of recurrences in patients with seminoma.

Most published series documenting the successfulness of surveillance for seminoma patients have only used CT abdomen rather than a CT abdo/pelvis[2,3]. However some institutional protocols for CT abdomen may not include all of the retroperitoneal nodes, and therefore in the absence of a testis cancer-specific protocol a CT abdo/pelvis is recommended here.

Centres are encouraged to establish a testis cancer-specific CT protocol aiming to detect enlarging nodes within the retroperitoneum (from the upper abdomen to the proximal external iliac region). An optimal scan should cover only from the diaphragm to the ischium, using low- dose CT without IV contrast, and be interpreted by a trained radiologist.

The phase III TRISST study demonstrated non-inferiority of three CT scans (at time points; 6, 18 and 36 months) compared to seven (at 6, 12, 18, 24, 36, 48, and 60 months)[4]. The three-scan cohort had numerically more relapses (2.0% increase, ITT) and 2.8% more Royal Marsden Hospital stage ≥IIC relapses compared to the seven-scan protocol. Whilst the stage ≥IIC relapses were within the non-inferiority margin (5.7%), 4/9 of these relapses could have been detected earlier by a seven-scan protocol, this is of particular relevance given the option for retroperitoneal lymph node dissection (RPLND) for stage IIA or IIB seminoma ≤3cm[5]. Whilst non-inferiority was demonstrated (seven vs three scans p= 0.389) and survival approached 100% in all study cohorts (median follow-up 6 years)based on consensus opinion, we recommend not omitting the final 60month scan.
MRI imaging of the retroperitoneum was also non-inferior to CT imaging (CT vs MRI p=0.342) and there were numerically fewer relapses with MRI surveillance compared to CT (0.6% versus 2.6%; decrease of 1.9%, 90% CI, –3.5 to –0.3). MRI surveillance can be considered a safe alternative to CT imaging however remains unfunded for this indication in Australia. Based on emerging data consider:
a) reducing imaging frequency to 6/18/36/60 months post-orchiectomy
b) omission of pelvic imaging in individuals who have *not* undergone prior pelvic surgery (including orchidopexy), and
c) use of MRI as an alternative to CT

Follow up beyond 5 years detects approximately 2-5% of all recurrences, representing between 0.2-1% of the patients at risk [2]. The value of follow up beyond 5 years and interval imaging beyond this point is uncertain. Some clinicians recommend annual follow up beyond 5 years, with a CT abdomen/pelvis at 10 years, although this is not part of recently published consensus recommendations[2,3]. At a minimum the authors recommend coordination with the local doctor and instructions on symptoms of possible recurrence, cardiovascular risks (if patient given chemotherapy), and a check of testosterone at 10 years[6,7].

Stage I Non seminoma

A CT chest must be performed at baseline to exclude higher stage disease, but is not recommended for ongoing surveillance. Chest imaging with a CXR is acceptable at the same time a CT abdomen/pelvis is performed. A CXR will uniquely detect 1% of recurrences[2]. Centres are encouraged to establish a testis cancer-specific protocol aiming to detect enlarging nodes within the retroperitoneum as for seminoma above.

Follow up after 5 years is not recommended as routine for NSGCT stage 1 patients. Approximately 1-2% of relapses occur after this time, representing 0.3-0.5% risk for the overall population who embark on a surveillance program[2].

The risk for recurrence of stage 1 NSGCT treated with 1 or 2 cycles of BEP is approximately 3%. The role of adjuvant chemotherapy versus surveillance in patients with risk factors for recurrence (LVI, embryonal predominance) is covered elsewhere[8,9]. Patients with lympho-vascular invasion who undergo surveillance are recommended to have monthly visits for 6 months in the first year. In patients who undergo chemotherapy, given the low risk of recurrence it is appropriate to reduce the frequency of visits, and this is outlined above.

Hormonal status

Patients are at risk of hypogonadism after orchidectomy[7]. Assessment of testicular function with testosterone (free, total), LH, and FSH are advised at 3 time points over five years. This is best done first thing in the morning to ensure accuracy of the assessment of the testosterone[10]. However the risk of hypogonadism does increase after five years, and a further test should ideally be performed at 10 years[7], organised by the local doctor.

References:

1 Conduit, C. *et al.* Patterns of Relapse in Australian Patients With Clinical Stage 1 Testicular Cancer: Utility of the Australian and New Zealand Urogenital and Prostate Cancer Trials Group Surveillance Recommendations. *JCO Oncol Pract*, Op2300191, doi:10.1200/op.23.00191 (2023).

2 Kollmannsberger, C. *et al.* Patterns of relapse in patients with clinical stage I testicular cancer managed with active surveillance. *J Clin Oncol* **33**, 51-57, doi:10.1200/jco.2014.56.2116 (2015).

3 Mortensen, M. S. *et al.* A nationwide cohort study of stage I seminoma patients followed on a surveillance program. *Eur Urol* **66**, 1172-1178, doi:10.1016/j.eururo.2014.07.001 (2014).

4 Joffe, J. K. *et al.* Imaging Modality and Frequency in Surveillance of Stage I Seminoma Testicular Cancer: Results From a Randomized, Phase III, Noninferiority Trial (TRISST). *J Clin Oncol* **40**, 2468-2478, doi:10.1200/jco.21.01199 (2022).

5 Stephenson A, B. E., Bixler BR, et al. Diagnosis and treatment of early-stage testicular cancer: AUA Guideline amendment 2023. *J Urol* (2023).

6 Haugnes, H. S. *et al.* Cardiovascular risk factors and morbidity in long-term survivors of testicular cancer: a 20-year follow-up study. *J Clin Oncol* **28**, 4649-4657, doi:10.1200/jco.2010.29.9362 (2010).

7 Sprauten, M. *et al.* Longitudinal serum testosterone, luteinizing hormone, and follicle-stimulating hormone levels in a population-based sample of long-term testicular cancer survivors. *J Clin Oncol* **32**, 571-578, doi:10.1200/jco.2013.51.2715 (2014).

8 Daugaard, G. *et al.* Surveillance for stage I nonseminoma testicular cancer: outcomes and long-term follow-up in a population-based cohort. *J Clin Oncol* **32**, 3817-3823, doi:10.1200/jco.2013.53.5831 (2014).

9 de Wit, R. Optimal management of clinical stage I nonseminoma: new data for patients to consider. *J Clin Oncol* **32**, 3792-3793, doi:10.1200/jco.2014.56.5747 (2014).

10 Rosner, W., Auchus, R. J., Azziz, R., Sluss, P. M. & Raff, H. Utility, Limitations, and Pitfalls in Measuring Testosterone: An Endocrine Society Position Statement. *The Journal of Clinical Endocrinology & Metabolism* **92**, 405-413, doi:10.1210/jc.2006-1864 (2007).