Quality measures in cervical lymphadenectomy for cutaneous malignancy by head and neck trained general surgeons

Fouad Nahab, Sita Ollek, Richard Harman, Richard Martin

ABSTRACT

AIM: Therapeutic lymphadenectomy remains the gold standard for surgical management of clinically evident regional cervical disease for cutaneous malignancy. However, international consensus on adequate lymphadenectomy is lacking. Attempts have been made to establish quality measures; suggested benchmarks for minimum and average nodal yield, as well as recurrence and complication rates have been quoted. We aim to compare our key performance indicators to those benchmarks published in the literature.

METHODS: This is a retrospective observational study conducted with prospectively maintained data, over an 11-year period (2007–2018).

RESULTS: Of 91 cervical lymphadenectomies included, mean nodal yield for ≤3 and ≥4 dissection levels were 19.7 and 38.7 respectively. We observed a combined locoregional recurrence rate of 25%. Subgroup analysis for melanoma (60) and cSCC (28) revealing regional nodal recurrence of 15% and 11%, respectively. We observed a 38.5% complication rate; however, less than 5.5% was considered grade IIIb/IIIb (Clavein-Dindo). Median follow-up of 19.3 months, five-year survival rate of 38% and 32% for melanoma and cSCC, respectively.

CONCLUSION: Our data indicates that we are meeting quality measures, set by higher volume centres. We believe that any surgeon with subspecialty training in head and neck surgery can meet quality measures with regards to cervical lymphadenopathy for cutaneous malignancy.

Therapeutic lymph node dissection (TLND) remains the gold standard for the surgical management of clinically evident regional cervical disease in patients with cutaneous malignancy. While the recommended minimum nodal yield is well established for certain malignancies (eg, gastric cancer, colon cancer), there is no consensus on what constitutes an adequate lymphadenectomy for cutaneous malignancies such as melanoma. In national and international published guidelines, such as the New Zealand Ministry of Health proposed melanoma management standards (2013), the Australian Cancer Council Clinical Practice Guidelines on Diagnosis and Management of Melanoma (2018), and the National Comprehensive Cancer Network guidelines (2019), there has been no consensus on the recommended minimum nodal yield for TLND in cutaneous malignancy.

To establish quality standards for cervical lymphadenectomy, a recommended minimum nodal yield has been published by other groups, but these recommendations have varied in the literature. The Wellington regional multidisciplinary Melanoma unit has also previously proposed minimum nodal targets of regional node dissections, advocating these provide strong prognostic and survival information. Additionally, it is well established that the lymph node ratio (LNR), defined as the proportion of positive lymph nodes over the nodal yield, is predictive of prognosis in various malignancies including melanoma and colorectal cancer.
The LNR may therefore prove useful in prognostication following TLND. While it has been shown that a complete lymphadenectomy does not impart a significant survival benefit compared to clinical observation in those patients with SLNB positive disease; it is still valuable in providing prognostic information, improving regional nodal control and allowing access to new adjuvant systemic treatment options.\textsuperscript{13,14}

To standardise surgical care and establish quality standards, key performance indicators (KPIs) have been proposed by high volume centres where benchmarks for nodal dissection have been reported. The Sydney Melanoma Unit (now Melanoma Institute Australia—MIA) has demonstrated that in their centre, the 90\textsuperscript{th} percentile for nodal yield of ≤3 and ≥4 level neck dissections were ≥6 and ≥20 lymph nodes, respectively.\textsuperscript{9} The literature further supports the benefit of achieving a minimum nodal yield and highlights the staging information it provides. For example, Rossi et al (2014) demonstrated that a higher number of excised lymph nodes was associated with better prognosis and recommended a minimum nodal yield of ≥7 and ≥14 nodes for ≤3 and ≥4 level cervical lymphadenectomies respectively, in order to more accurately stage patients using the American Joint Committee on Cancer (AJCC) guidelines.\textsuperscript{10}

A regional lymphadenectomy is a standardised dissection, the extent of which is determined by pre-defined anatomic boundaries, node levels at risk and radiological imaging. The American Academy of Otolaryngology—Head and Neck Surgery provide standardised anatomical boundaries to determine the level of dissection, for both therapeutic lymphadenectomy and selective lymph node dissections.\textsuperscript{15} Although cadaveric and radiological studies have demonstrated that on average there are at least 28 lymph nodes on each side of the neck,\textsuperscript{16,17} variation exists in the extent of nodal dissection and the resulting nodal yield. Factors contributing to this variation include modifications based on an anatomic area, patient anatomy, surgical technique and thoroughness of histopathologic analysis.\textsuperscript{18,19} In addition, surgeon experience and clinical judgment based on the individual clinical scenario is an important factor in determining the volume of tissue harvested and from which levels, as is done with a selective nodal dissection in the head and neck region. This is well demonstrated by recent research which reinforces the trend to safely omit level 1 and 4 when operating on patients with clinically apparent parotid melanoma metastases, allowing the surgeon to take ≤3 levels of lymph nodes in their neck dissection.\textsuperscript{20}

With data published from MSLT-II, a positive SLNB is no longer an indication for an immediate lymphadenectomy.\textsuperscript{12} However, at the present time a therapeutic lymphadenectomy remains the standard of care for clinically evident regional disease.\textsuperscript{4,12} Previous literature on cervical nodes from the MIA has also demonstrated the significance of nodal positivity as one of the most important factors (alongside Breslow thickness) in determining survival in melanoma patients with nodal metastases in the head and neck region.\textsuperscript{21} Lymphadenectomy is not without risk and carries potential morbidity. The frequency and severity of postoperative complications is another important metric for quality assurance. The complication rate following cervical lymphadenectomy is reported in the literature to be between 8\% to 39\%; and included wound complications (bleeding, seroma, infection) in addition to transient and permanent nerve damage.\textsuperscript{22,23} Striving to minimise morbidity following cervical lymphadenectomy is an important part of maintaining high-quality care.

Melanoma and non-melanoma skin cancer (NMSC), mainly cSCC, are cutaneous malignancies for which cervical lymphadenectomies are commonly performed.\textsuperscript{24,25} New Zealand has the highest rate of cutaneous melanoma in the world (51.8 per 100,000) and Auckland has the highest incidence of NMSC (1,906 per 100,000). International research has indicated that incidence of melanoma in New Zealand is projected to rise within the next decade, and we still carry the highest age-standardised melanoma mortality rates.\textsuperscript{26–28} Waitematā District Health Board (WDHB) is located in Auckland City, and is the largest district health board in New Zealand; servicing more than 620,000 people.\textsuperscript{29} Given the high volume of disease being treated within our district health board, we wished to assess the quality of cervical lymphadenectomies being
performed. We aimed to evaluate outcomes including nodal yield, complications, recurrence and all-cause mortality in patients undergoing cervical lymphadenectomies for melanoma and NMSC over an 11-year period by general surgeons with subspecialty training in head and neck surgery.

**Method**

**Objectives**

Our primary objective was to determine the mean and minimum nodal yield obtained with cervical lymphadenectomies and to compare this to published literature. Secondary objectives were to assess quality standards including overall survival, complication rate, in addition to local, regional nodal and distant recurrence rates.

**Patients and methods**

This retrospective observational study is based on a prospectively maintained database from the WDHB and Melanoma Unit. We included patients who underwent a cervical lymphadenectomy between 2007–2018 for cutaneous malignancies with regional cervical metastases. Neck dissections involving parotidectomy were identified and provided a ‘parotid nodal’ category. Dissections included patients with clinically occult (ie, identified on SLNB) or clinically evident (ie, palpable or radiographically detected) regional nodal disease. Operations were performed by one of two general surgeons with subspecialty training and experience in head and neck surgery. All cases were discussed through a regional multidisciplinary meeting. Patients underwent routine postoperative follow-up at two weeks following surgery, then intermittently for 3–4 months. This research was approved by institution locality process (Awhina).

**Statistics**

We analysed data points of interest using descriptive statistics; and included age, gender, date of surgery, date of death where applicable, primary diagnosis, type of procedure, primary tumour site, Breslow thickness, nodal yield, number of positive lymph nodes, extracapsular spread, postoperative complications, adjuvant radiotherapy, as well as local, regional and distant recurrence. Oncologic outcomes including mortality and recurrence rate were analysed separately for melanoma and cSCC. Lymphadenectomies were categorised as ≤3 dissection levels versus ≥4 dissection levels. We compared the nodal yield from both ≤3 and ≥4 level dissections to the findings by the Spillane group, who demonstrated that their 90th percentile nodal yield for ≤3 and ≥4 level dissections were ≥6 and ≥20 lymph nodes, respectively.

Flow charts and tables were created using Google documents and Lucidchart. Chi-squared test was conducted to assess statistical significance using Graph-Pad Prism 8.3.1 software. Melanoma stage was assigned based on the AJCC (8th edition).

**Results**

Ninety-one cervical lymphadenectomies were performed in patients with metastatic disease to cervical lymph nodes, with all but one being unilateral dissections. For the bilateral case, we treated nodal yield from each side separately. The median age at time of surgery was 72 years (mean: 71 years, SD 13.8, range 21–94); there was a male predominance with 74 males (81%), compared with 17 females (19%) (Table 2). Melanoma was the most common primary malignancy, accounting for 66% (60/91) of patients. cSCC was the second most common

<table>
<thead>
<tr>
<th>Histological diagnosis</th>
<th>n</th>
<th>Proportion</th>
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<tbody>
<tr>
<td>Melanoma</td>
<td>60</td>
<td>66%</td>
</tr>
<tr>
<td>SCC</td>
<td>28</td>
<td>31%</td>
</tr>
<tr>
<td>MCC</td>
<td>1</td>
<td>1%</td>
</tr>
<tr>
<td>Cutaneous mucinous carcinoma</td>
<td>1</td>
<td>1%</td>
</tr>
<tr>
<td>Adnexal tumour</td>
<td>1</td>
<td>1%</td>
</tr>
<tr>
<td>Total</td>
<td>91</td>
<td></td>
</tr>
</tbody>
</table>
primary malignancy at 31% (28/91). There were three other primary malignancies: Merkel cell carcinoma (MCC), primary cutaneous mucinous carcinoma, and one case of an adnexal tumour (Table 1). Patients with melanoma were categorised as stage IIIA, IIIB, IIC and IIID in 10%, 24%, 54% and 7% of cases respectively, according to the AJCC.

There were three patients (5%) with stage IV melanoma (Figure 1). The stage IV melanoma cases were two palliative dissections in the context of non-regional metastatic disease, and one curative dissection having previously had an axillary dissection with now palpable cervical metastases.

Table 2: Demographics for patients undergoing cervical lymphadenectomy.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Number (mean)</th>
<th>Proportion</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age (years)</td>
<td>73 (71.3)</td>
<td>-</td>
<td>21-94</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>74</td>
<td>81%</td>
<td>-</td>
</tr>
<tr>
<td>Female</td>
<td>17</td>
<td>19%</td>
<td>-</td>
</tr>
<tr>
<td>Primary tumour site</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Head + neck</td>
<td>64</td>
<td>70%</td>
<td>-</td>
</tr>
<tr>
<td>Torso</td>
<td>15</td>
<td>16.5%</td>
<td>-</td>
</tr>
<tr>
<td>Upper limb</td>
<td>5</td>
<td>5.5%</td>
<td>-</td>
</tr>
<tr>
<td>Unknown primary site</td>
<td>7</td>
<td>8%</td>
<td>-</td>
</tr>
</tbody>
</table>

Figure 1: Proportion of melanoma by stage (%)—based on AJCC 8th Edition.
Thirty-two cases included cervical dissection of ≤3 levels, and 59 cases were dissection of ≥4 levels (Figure 2). The median nodal yield in ≤3 dissection levels was 27 (mean: 19.7, SD 17.1, range 6–48). The median nodal yield in ≥4 dissection levels was 35 (mean: 38.7, SD 17.4 range 15–76). All patients who underwent a ≤3 dissection had a nodal yield of six or more lymph nodes. Among those who underwent ≥4 dissection levels, 88% (52/59) had ≥20 lymph nodes removed. The overall mean and median LNR for all patients were 12% (SD 0.15) and 6% respectively. The mean LNR was lower for patients with melanoma (10%) when compared to those with SCC (14%). Of the 91 neck dissections, 31% included superficial or complete parotidectomy. The median number parotid lymph nodes dissected was 1 (Mean: 2.6, SD 2.2, range 1–8). 90% of our ≤3 level dissections, and ≥4 level dissections contained ≥8 and ≥19 lymph nodes, respectively.

With a median follow-up duration of 19.4 months (mean 29 months, SD 30.9, range 0.5–130), locoregional recurrence occurred in 25% of patients (23/91). Of the 91 lymphadenectomies included in the study, 13% had regional nodal recurrence.

The overall complication rate was 38.5%, with a total of 35 complications. Transient neuropraxia was the most common complication, occurring in 13 patients (14%), of which 11 involved a branch of the facial nerve (CNVII), and two involved the spinal accessory nerve (CNXI). Formation of a seroma or hematoma occurred in 11 patients (12%). Other complications included wound breakdown or infection, chyle leak and permanent nerve palsy (Table 3). One patient developed a postoperative pneumomediastinum which was self-limiting. Most complications were managed in an outpatient setting and did not require operative intervention. A total of five patients (5.5%) patients experienced complications considered as Grade IIIb/IIIb(d) Clavien-Dindo classification. Of these five patients; one developed a postoperative haematoma requiring evacuation in theatre; another a suppurative wound infection requiring operative drainage and washout. 3.3% had permanent cranial nerve palsy (3/91), two cases of facial nerve (CNVII) and one of accessory nerve (CNXI) impairment. No postoperative deaths were observed. During the follow-up period, all-cause mortality rate was 56% (51/91).

![Image](image-url)  
**Figure 2**: Flowchart of cervical dissections.

SCC: Cutaneous squamous cell carcinoma.
Melanoma patients

In those patients who underwent a cervical lymphadenectomy for regional metastatic melanoma, 16 patients (26.7%) developed some form of disease relapse; locoregional recurrence. However, the rate of nodal recurrence alone was 15% (9/60) in the melanoma group overall. All patients who developed a local and/or regional nodal recurrence also eventually developed distant metastatic disease. Overall, 38 patients (63%) developed distant metastatic disease, with 22 (58%) of these patients developing distant metastatic disease without evidence of locoregional recurrence. Twenty-six (36.7%) patients remained disease free at the time of last follow up.

From this group, 55% (33/60) received postoperative radiotherapy. We observed a regional nodal recurrence rate of 15.2% (5/33) in those receiving radiotherapy. This is compared to 14.8% (4/27) recurrence rate in the no-radiation group. There was a statistically significant higher rate of extra-capsular spread in the radiotherapy group compared to the no-radiotherapy group, 66% vs 30% (p=0.043, Chi square 8.148), respectively. In addition, there was a greater mean positive node in those undergoing radiotherapy vs no-radiotherapy, 4.0 (SD 4.59, 0–21) vs. 1.6 (SD 4.73, 1–4). Regional nodal recurrence rate for clinically occult and clinically detectable disease was 6% and 19% respectively; and reflect a completion lymph node dissection (CLND) in 33.3% of cases (20), compared to TLND in 66.7% of cases (40).

The all-cause mortality rate of patients with melanoma was 50% (30/60), within the follow-up period of the study; with a five-year overall survival rate of 38% (Figure 3). The mortality rate did not differ significantly between those with clinically occult (47%) versus clinically detected (51%) regional disease (p=0.71, Chi-squared = 0.1372).

Table 3: Complications by type.

<table>
<thead>
<tr>
<th>Complication</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chyle leak</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Nerve injury (transient)</td>
<td>13</td>
<td>14</td>
</tr>
<tr>
<td>Permanent palsy</td>
<td>3</td>
<td>3.3</td>
</tr>
<tr>
<td>Seroma/haematoma</td>
<td>11</td>
<td>12</td>
</tr>
<tr>
<td>Wound infection</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Other</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>35</td>
<td></td>
</tr>
</tbody>
</table>

Figure 3: Kaplan-Meier Survival Curve: melanoma by stage IIIA, B, C, D and IV.
Squamous cell carcinoma

Among the 28 patients with a primary cSCC, postoperative disease relapse (locoregional recurrence) occurred in seven patients (25%). However, the rate of regional nodal recurrence alone in this group was 11% (3/28) overall. One quarter of these patients (25%) with local or regional nodal recurrence also developed distant metastases.

Of the cSCC group, 82% (23/28) underwent postoperative adjuvant radiation therapy. We observed a statistically significant reduction in regional nodal recurrence rate with the use of adjuvant radiotherapy (4% with radiotherapy vs 40% without radiotherapy) (p=0.02, Chi square = 5.46). The distant metastatic rate was 28.5%, and all-cause mortality for those undergoing cervical lymphadenectomy for metastatic cSCC was 67.9% (19/28); we observed a five-year survival rate of 32% in this group.

Discussion

Surgery continues to play a key role in the treatment of patients with lymph node metastases from cutaneous malignancies and remains the gold-standard in those with clinically evident disease.22,23 While a thorough surgical dissection is imperative, this must be balanced against the potential for morbidity and risk of complication. It is important that standards are set and followed to ensure provision of adequate surgical resection while minimising morbidity during such a procedure.4

While what constitutes an adequate regional cervical lymphadenectomy remains undefined, a proposed measure of quality assessment is the minimum nodal yield. The nodal yield is a combined surgical and pathology key performance indicator. The MIA has suggested a benchmark nodal yield average of 19.5 lymph nodes (median 18.5) for cervical lymphadenectomies with ≤3 dissection levels or an average 38.9 (median 36) for ≥4 dissection levels. Moreover, a minimum nodal yield of ≥6 lymph nodes for ≤3 cervical dissection levels, and ≥20 lymph nodes for cervical lymphadenectomy dissection of ≥4 levels has been proposed, using the 10th percentile as a cut-off metric.9 Our series has met this standard of quality assurance, reaching a median nodal yield of 27 (mean 19.7, SD 17.08, range 6–48) for ≤3 dissection levels and 35 (mean 38.7, SD 17.42 range 15–76) for ≥4 dissection levels. We have also met the recommended benchmarks for minimum nodal yield, in 100% of our cervical lymphadenectomies involving ≤3 dissection levels, and in 88% of those involving ≥4 or more dissection levels. Although our data would suggest a minimum recommended nodal yield of ≥8 nodes, and ≥20 nodes for ≤3 and ≥4 level dissections, respectively and is based on the 10th percentile metric. We have aligned our minimum nodal yield metric of the 10th percentile with previously published research, as this metric is reproducible across institutions, and accounts for minimal nodal yield with respect to the extent of surgery within each nodal field. Use of this 90% threshold helps to identify those cases of inadequate lymph node retrieval and ensures institutions continue to achieve a high benchmark. Although, previously published literature on minimal nodal yield has also been based on expert opinion, with a figure of minimum 15 nodes for cervical neck dissections published by the Bilimoria group which include ≤3 and ≥4 dissection levels.9,10,32

Previous research has reinforced the importance of LNR as an independent prognostication tool, highlighting the improved survival in those cases with LNR ≤10%.12,23 Our overall mean LNR was 12%, with a difference in mean LNR for melanoma and SCC, 10% and 14%, respectively. Furthermore, it has been shown specifically for head and neck regional metastatic melanoma, that the most important factors predicting survival were nodal positivity in addition to Breslow thickness.21 Published cervical lymphadenectomy complication rate ranges from 8.3 to 39.0%.11,22,23 Our complication rate of 38.5% reflects all complications, including those which did not require readmission or re-operation and lines up with the type of complications encountered in the literature. The majority were temporary cranial nerve neuropraxias followed by operative site seroma. Less than 5% of our complications are considered Grade IIIb/IIIb(d).31 There were no complications grade IV or higher. Only 3.3% (3/91) had permanent neuropraxia. Our findings are in keeping with previously published benchmarks on acceptable complication rates from the MIA, which quotes an acceptable rate of less than 5% for re-intervention for wound complications following
cervical lymphadenectomy; and <50% and <20% temporary and permanent cranial nerve palsy rate, respectively.34

Another important aspect of quality assurance is regional disease control following lymphadenectomy. The Chan group reported a regional recurrence rate of 56% (86/153) following cervical lymphadenectomies for metastatic melanoma.35 And previous work by the Geltzeiler group has demonstrated a regional recurrence rate of 29% in cervical lymphadenectomy for metastatic melanoma.21,24 In work by another National unit, combined local and regional recurrence rates have been reported as 30% for cervical TLND of stage III melanoma.11 Data from the Martin group (2012) has demonstrated a combined locoregional recurrence rate of 27.6% following cervical TLND in head and neck melanoma; further breakdown revealed a lymph node recurrence of 8.5%.21 We have identified an overall disease relapse (locoregional recurrence) rate of 25%; however, this was further analysed to account for differences in disease characteristics for melanoma compared to SCC, with emphasis on regional nodal recurrence. Subgroup analyses of our regional nodal recurrence revealed a rate of 15.0% and 10.7% for melanoma and SCC, respectively. Overall this reflects an accurate and reproducible surgical practice and is comparable to rates previously reported in the literature.11,21,24,35

Our observed regional nodal recurrence rates following radiation therapy differed between the SCC and melanoma groups. There was a significant reduction in nodal recurrence following radiation therapy in the cSCC group (4%), compared to 40% recurrence in those not undergoing postoperative radiation therapy. This result is based on a small dataset and requires a larger sample size to see a true effect. In the melanoma group, the radiotherapy vs no-radiotherapy group had similar nodal recurrence rates (15.2% vs. 14.8%, respectively). The patients in these two groups cannot be directly compared due the higher risk of nodal recurrence carried in the radiotherapy group, seen with a greater rate of ECS and greater mean positive nodes, compared to the no-radiotherapy group. This result highlights the effect of radiotherapy at reducing risk of nodal recurrence, as seen in the high risk (radiotherapy group) sustaining similar rates of recurrence in the lower risk group (no-radiotherapy).

This result aligns with well-established evidence that radiotherapy has an approximately 10% reduction in nodal recurrence for melanoma patients following therapeutic lymphadenectomy.14

Our centre provides head and neck oncological resection services to the WDHB which is expected to serve a projected population of 628,970 by 2019. Of this demographic, a large proportion of the population (31.7%) are aged 50 years or older.29 Although there is a lack of consensus in regional and international guidelines on the minimum recommended nodal yield for cervical lymphadenectomies performed for cutaneous metastases, we can still assess quality standards against those recommended by higher volume centres.6,7 Here we have demonstrated that the nodal yield for cervical lymphadenectomies in our centre is in keeping with the proposed benchmarked quoted in the literature.5,11 Furthermore, our complication rate is similar to that which has previously been published.

Quality measures or KPIs are an important metric when dealing with low-volume surgical procedures. The number of nodal dissections for melanoma has dramatically reduced since the practice changing results from MSLT-II.13 If KPIs are not met then node dissection cases should be referred to tertiary referral centres that are meeting KPIs, but who also have the appropriate perioperative support; for example, nurse specialists, and lymphoedema physiotherapists. Our results show a 42% survival at 19.3-month median follow-up based on surgical treatment only. We are now entering a very interesting period with adjuvant and neoadjuvant anti-PD1 or BRAF/MEK systemic treatment which will no doubt improve survival in these high-risk melanoma patients.36–39

We recommend a minimum nodal yield of 8 for ≤3 level and 19 for ≥4 level dissections for cutaneous malignancies, using the 10th percentile cut-off metric. We believe that any surgeon with subspecialty training in head and neck surgery can meet quality assurance standards with regards to cervical lymphadenectomy for cutaneous malignancy. Until a consensus is reached on the accepted quality standards for regional lymphadenectomies, we must routinely audit and compare our performance to the currently published recommendations to ensure we are providing the best possible care.33
Competing interests:
Nil.

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WDHB, Department of General Surgery, Melanoma Unit.

Author information:
Fouad Nahab, Surgical Registrar, Department of General Surgery, North Shore Hospital, Waitemata District Health Board, Takapuna, Auckland; Sita Ollek, Surgical Oncology Fellow, Department of General Surgery, North Shore Hospital, Waitemata District Health Board, Takapuna, Auckland; Richard Harman, General Surgeon, Department of General Surgery, North Shore Hospital, Waitemata District Health Board, Takapuna, Auckland; Richard Martin, General Surgeon, Department of General Surgery, North Shore Hospital, Waitemata District Health Board, Takapuna, Auckland.

Corresponding author:
Fouad Nahab, Department of General Surgery, North Shore Hospital, 124 Shakespeare Road, Takapuna, Auckland.
f_nahab@hotmail.com

URL:

REFERENCES:


