THE NEW ZEALAND MEDICAL JOURNAL
Journal of the New Zealand Medical Association

Outcomes for differentiated thyroid cancer in New Zealand: comparison of South Island and Auckland data

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Brownlie and colleagues[1]—in this issue of the *NZMJ*—have reviewed the outcomes of the bulk of the New Zealand South Island cases of differentiated thyroid cancer (DTC) seen between 1984 and 2009; a total of 411 cases. Twenty-five patients or 6% of the total died, compromising twice as many women as men, with a mean age of 65 years. The patients were operated on by 19 different surgeons and no patient less than 45 years of age died. All deaths were in Caucasian patients, and 15 of the 25 were incurable from the outset as a result of locally advanced unresectable disease or metastatic disease at diagnosis.

According to Table 1, local failure in the neck occurred in 9 or 36% of their patients. The ratio of females to males who died was similar to the gender ratio for all differentiated thyroid cancer (DTC) patients: 2.1:1 favouring females.

Table 1. Prognostic effects of extra-thyroid extension and regional disease on outcome

Variables	T4A N0/n1a	T4A N1b	T1-3 N1b
A&W	56% 11/18	40% 10/25	77% 17/22
N1 Rec	66% 9/18	13% 2/25	18% 4/22
AWD	22% 4/18	50% 9/25*	9% 2/22
DOD	0	20% 5/25*	5% 1/22

N0 no regional disease, **N/1a** central compartment disease; **N1b** lateral neck disease, **A&W** alive & well; **N1 Rec** recurrence in lateral neck; **AWD** alive with disease; **DOD** dead of disease. *Significantly different to both the other groups p<0.04 or better; **T4A** extra-capsular spread.

The editorial author has reviewed his personal experience of over 2000 thyroidectomies performed in Auckland between 1984 and 2012; 300 patients had differentiated thyroid cancer.

The patients treated between 1984 and 2007 have been analysed. These data have been presented both nationally and internationally but never published. Statistical analysis utilised Chi-squared analysis. Patients were staged in accord with The Mayo Clinic staging MACIS,[2] and also using the guidelines from the Joint American Staging System for Thyroid Cancer.[3]

Lymph node status (levels 1–7) was as described by Memorial Sloan Kettering Cancer Centre.[4,5] There were 127 DTC patients aged <45 years (97 papillary, 30 follicular), and 123 aged >45 years (94 papillary, 29 follicular).

The ethnic distribution was similar for the two age groups with Europeans making up 61%, Māori 13%, Asian 15%, and Pacific 14%. Longest follow-up (FU) is 25 years with mean FU 13 years.

The vast majority of patients were treated with total thyroidectomy. Over recent years central node dissection (level 6) has been almost universally performed for papillary cancer or follicular variant of papillary cancer in order to achieve lower recurrence rates in the central compartment and to have a higher percentage of patients with post-op thyroglobulin levels approximating zero.[6]

In addition for patients with lateral neck disease, neck dissection of levels 2–5 (after level 6 the commonest sites of involvement are in order levels 4,3 and 2 with level 5 being involved in >20% of patients) was employed for most patients.[5]

There are a number of differences in this Auckland experience when compared with the South Island report of Brownlie and colleagues;[1] in particular the following.

- In Auckland, major prognostic factors governing outcome were similar to those from The Mayo Clinic,[2] these included patient age, the presence of locally advanced disease, adequacy of resection, the status of regional disease, the completeness of the resection performed.
- In addition, in Auckland the ethnicity of the patient was significant with Asian patients having the best outcomes while Pacific patients had the worst outcome especially male Pacific patients aged >45 years.[7]
- Age was a strong prognostic indicator for both recurrence and death in accord with Mazzaferri and Jhiang.[8] Recurrence was frequent in young patients and in older patients with the lowest rate of recurrence in middle aged patients. In contrast, DOD and the presence of unfavourable bone mets were largely confined to patients over 60 years of age. See Figure 1.

Abbreviations used in the following figures and tables

N0 no regional disease, **N1b** lateral neck disease, **N/1a** central compartment disease

Rec recurrence, **N1 Rec** Recurrence in lateral neck

Mets metastatic disease, **M1 Rec** develop metastatic disease

DOD dead of disease

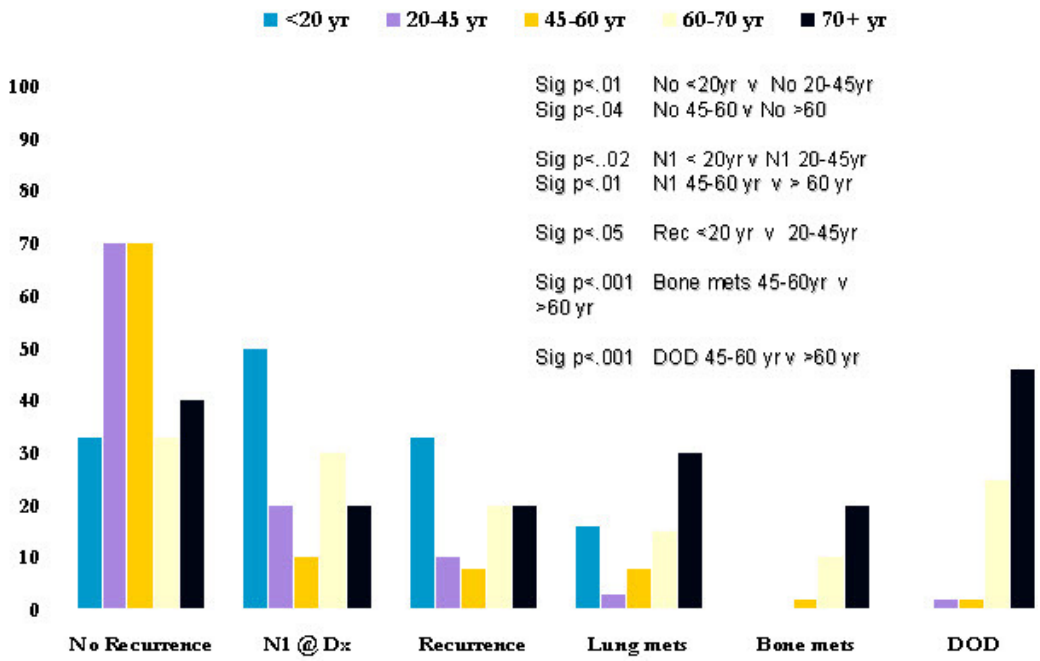
@ Dx at diagnosis

NS not statistically significant

AWD alive with disease, **A&W** alive & well

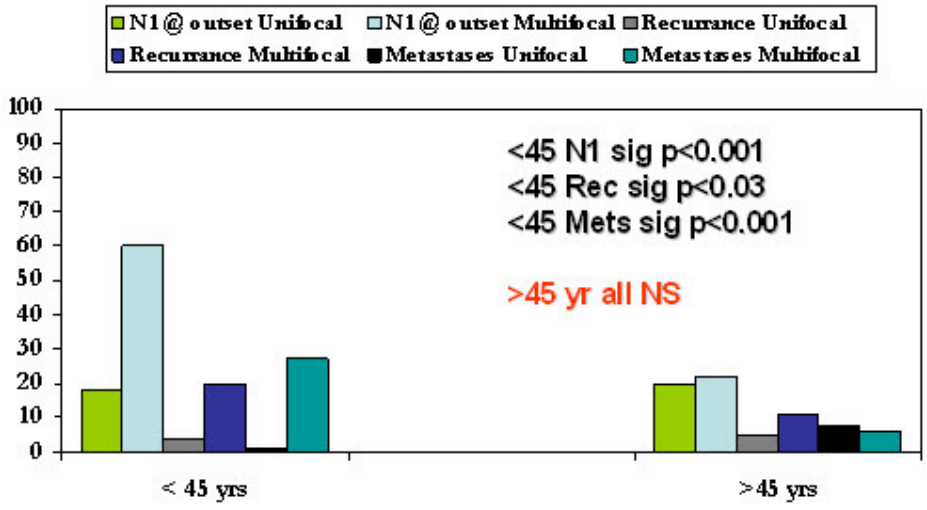
***** significance p<0.05 ****** significance <0.03 or better

Figure 1. Effect of age on outcome of papillary cancer



- Multifocal tumours were associated with less good outcome in patients < 45 years, but multifocality did not influence outcome in older patients. See Figure 2.

Figure 2. Multifocal papillary primary: influence of age



- Progressive increase in tumour size had only a minor effect on outcome, but extra-thyroid spread (T4a) had a major effect on outcome. See Table 2.

Table 2. Effect of tumour size and extra-capsular spread (T4A) on outcome

Size CM	T1 <2 cm	T2 2–4 cm	T3 >4 cm	T4A
A&W	96% 67/71	91% 78/80	80% 22/28	49% 21/43**
AWD	1% 1/71	0% 0/80	7% 2/28	30% 13/43**
DOD	0% 0/71	1% 1/80	0% 0/28	12% 5/43**

** Significant difference from other groups p<0.04 or better.

- In addition if there was lateral neck disease coupled with a locally invasive primary (Stage T4A N1B) then the outcome was significantly worse. See Table 2. This is in accord with the findings of Hay et al from The Mayo Clinic.[2]
- Also Table 2 demonstrates the relatively good outcome for regional disease when there is no locally invasive primary, the relatively good outcome when a locally invasive primary was not coupled with regional disease.
- For younger patients, the number of nodes involved impacted on recurrence. See Table 3. This is in accord with Sugatani et al.[9]

Table 3. Papillary cancer in patients aged <45 years of age: effect of >5 involved nodes

Variables	Nil or <5 Nodes	>5 Nodes
A&W	93 % 75/81	57% 8/14 P<0.001
N1 Rec	6% 5/81	29% 4/14 P<0.01
M1 Rec	1% 1/81	36% 5/14 P<0.001
DOD	1% 1/81	0% 0/14 NS

- In patients aged >45 years the size of nodes impacted significantly on both recurrence and survival. See Table 4. This finding is in agreement with Kitajiri et al.[10]

Table 4. Papillary cancer in patients aged >45 years: effect of nodes >3 cm diameter

Variables	No or nodes <3 cm	Nodes >3 cm
A&W	79% 59/75	38% 6/16 p<.001
N1 Rec	9% 7/75	19% 3/16 NS
M1 Rec	11% 8/75	43% 7/16 p<.001
DOD	1% 1/75	25% 4/16 p<.003

- Completeness of resection was a highly significant prognostic factor, as was the case at Mayo [Clinic].[2] Patients with extensive disease necessitating borderline resection of cancer involving trachea, larynx, oesophagus did significantly less well than when complete resection could be performed. See Table 5.

Table 5. Outcome: incomplete versus complete resection

Variables	Complete resection	Incomplete resection
A&W	74% 147/204	12% 3/26 p<0.01
LR Rec	1% 2/204	31% 8/26 p<0.01
AWMets	1% 2/204	62% 16/26 p<0.01
DOD	0.5% 1/205	27% 7/26 P<0.01

- Outcome as a function of race is shown in Table 6. The outcomes for Europeans, Māori, and Asians were similar irrespective of age, and the outcomes of Pacific patients aged <45 years were also similar to the above three ethnic groups.
- Asians were relatively over-represented (Asian population over the study period would have been much less than 50% of the Māori population[7]), and Asians had the best outcomes of any race with no patients either AWD or DOD.
- In contrast Polynesians aged >45 years fared significantly worse than other races largely due to the high proportion of males aged >65 years with T4A, N1b disease (6 patients), along with 4 Polynesian males with T4b disease, 3 of whom died of disease.

Table 6. Differentiated thyroid cancer (DTC) in all ages: ethnicity versus outcome

Variables	European	Asian	Māori	Pacific <45	Pacific >45
A&W	88% 127/144	100% 37/37	77% 14/18	73% 11/15	30% 6/20 p<0.03
AWD	10% 15/144	0%	22% 4/18	27% 4/15	45% 9/20 p<0.05
DOD	1% 2/144	0%	0%	0%	25% 5/20 p<0.03

- MACIS score (based on presence of Metastases, Age, Completeness of resection, Invasion and Size[2]) stratified patients for outcome. See Table 7.

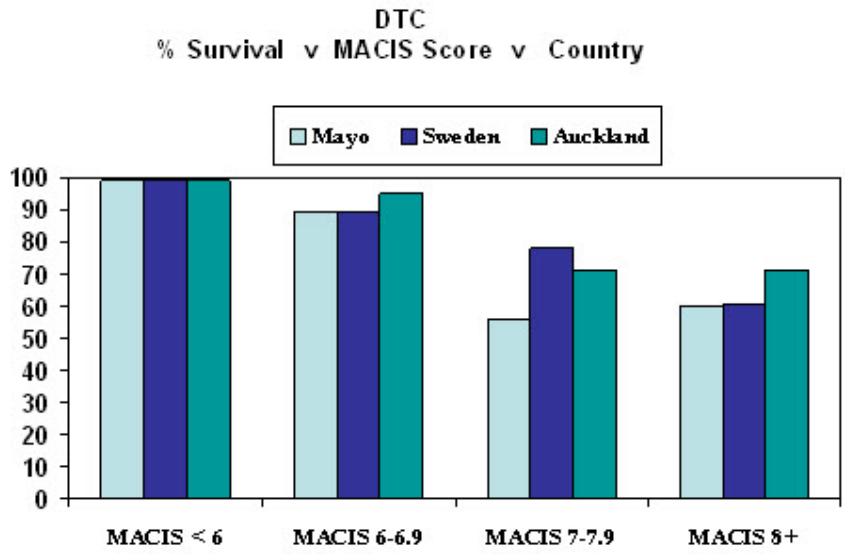
Table 7. Outcome of DTC in all ages versus MACIS score

MACIS Score	<6	6–7	>7
A&W	99% 185/187	66%* 16/24	21%* 5/24
AWD	0.5% 1/187	29%* 7/24	50%* 12/24
DOD	0.5% 1/187	4%* 1/24	29%* 7/24

* Significantly different to preceding MACIS value p<0.04 or better.

- When survival as a function of MACIS score for patients treated in Auckland, Mayo [Clinic],[2] and Sweden[11] were compared, the survival data were similar. See Figure 3. In addition, the percentage of patients with high MACIS score seen in Auckland was double that seen at Mayo.

Figure 3. DTC Outcomes of Mayo Clinic (USA) versus Sweden versus Auckland (NZ)



- Gender was unimportant in survival for any patient group. When all females were compared with all males the outcomes were virtually identical. See Table 8 below.

Table 8. DTC effect of gender on outcome: all female patients versus all male patients

Variables	Females	Males
A&W	88% 168/192	83% 40/48
AWD	8% 15/192	10% 5/48
DOD	5% 9/192	6% 3/48

Overall there are a number of differences in outcome for South Island patients versus North Island patients. This is largely explained on the one hand by the higher percentage of good prognosis Asian patients in the North Island coupled on the other hand with a higher proportion of poor prognosis Polynesian patients seen in Auckland, many of whom were referred from Samoa.

There is little doubt that most patients with differentiated thyroid cancer are best treated by total thyroidectomy and for papillary cancers a central neck dissection is also appropriate.[6]

An assessment of the roles of adjuvant radioiodine (RI) and external beam radiation (EBR) in the management of DTC is beyond the scope of this editorial. However it is this author's view that while RI is useful for treating metastatic thyroid cancer, data supporting its use as an adjuvant therapy in young patients with good prognosis lesions, is limited.[12]

Available World data indicate that RI may diminish recurrence in older patients with unfavourable prognostic factors.[12] In contrast, the data supporting the use of EBR to diminish recurrence in patients with unfavourable central or lateral compartment disease is more compelling,[12] and this modality is currently probably under-utilised in New Zealand for managing patients with locally advanced central and/or lateral neck disease.

Competing interests: None known.

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