Radical prostatectomy outcomes in a prostate cancer patient cohort managed by Public Hospitals in Auckland from 2006-2013.

Nishi Karunasinghe[1*], Sameer Bhat[1], Logan Carpenter[2], Jonathan Masters[3], Megan Goudie[4], Sue Osborne[5], Alice Wang[1], William Zhu[1], Lynnette R. Ferguson[6]

1.Auckland Cancer Society Research Centre, Faculty of Medical and Health Sciences, The University of Auckland, Private bag 92019, Auckland, New Zealand.
2.Anatomical Pathology and Cytology Department, LabPlus, Auckland, New Zealand, 3.Urology Department, Whangarei Hospital, Whangarei, New Zealand, 4.Urology Department, Auckland City Hospital, Auckland, New Zealand, 5.Urology Department, Northshore Hospital, Auckland, New Zealand,
6. Emeritus Professor, Faculty of Medical and Health Sciences, The University of Auckland, Auckland, New Zealand, 6.

Background

Recent studies show that 55% of prostate cancer (PC) diagnoses in Auckland New Zealand (NZ) were of high-risk nature. When considering PSA levels at the time of PC diagnosis, there is a delayed diagnosis of these high-risk cancers in Auckland, NZ men compared to that of US Europeans and US Africans[1]. This was exacerbated in ever-tobacco smokers and was compounded in ever-tobacco smokers carrying a particular genetic polymorphism variant, the *aldo-keto reductase 1C3* (*AKR1C3*) rs12529 G allele which is more common in Māori and Pacific ethnic groups[2]. Based on prospective monitoring of a group of PC cases managed with radical prostatectomy (RP), over-diagnosis has been defined as those with a Gleason Score (GS) of <7, a pathological stage of <pT2a, and negative surgical margins; and under-diagnosis as either a pathological stage of ≥pT3 or positive surgical margins (PSMs)[3]. The purpose of the current study was to report the status of the histological characteristics associated with prioritized ethnic groups as well as subsequent PC-related outcomes in a patient cohort after RP carried out at Public Hospitals in Auckland, NZ.

Methods

This retrospective cohort study involved patients recruited between October 2006 and December 2013 from the Auckland Region. Patients with any ethnicity with positive biopsies for PC aged between 45-90y were recruited for PC studies (n=515). Out of these men, those managed with any approach to RP at public hospitals (n=134) were considered for analysis. Ethnicity, BMI, lifestyle, NHI number, and clinical data were recorded at recruitment for all patients. All adjuvant and salvage therapies used in their management until December 2013 were also recorded. The post-RP histological data were extracted from the public hospital records. This cohort was longitudinally monitored for a median of 8.4y (IQR 7.1, 10.6) since RP for mortality recordings. These data were provided by the Analytical Services of the Ministry of Health aligned to a list of patient NHI numbers provided by us. Parameters were assessed with and without stratifications based on self-reported prioritized ethnicity. Continuous variables and categorical variables were tested using the Kruskal Wallis Analysis of Variance on Ranks and Fisher test respectively. A significance level of P<0.05 was set out for this analysis.

Results

A total of 279 (54.2%) out of the 515 patient participants underwent RP for management of their PC. Data related to a sub-cohort of 134 patients managed by the Auckland public hospitals are reported below. The general characteristics of this cohort are summarised in **Table 1**. None of the patient factors differed significantly between ethnicities at a P<0.05 level.

Table 1. General characteristics of the RP sub-cohort.

		Prioritised Ethnicity*				
Variable	All	Maori	Pacific-Peoples	European	Others	P value
Ethnicity, n (%)	134 (100)	7 (5.2)	5 (3.7)	117 (87.3)	5 (3.6)	-
BMI kg/M², median (IQR)	27.0 (25.0, 30.0)	29 (28,32)	28 (28, 31)	27 (25,30)	25 (24, 25.3)	0.06[a]
Ever-smoker %	52.2	42.8	60	51.3	75	0.79[b]
Alcohol consumer %	44.8	42.8	60	44.3	60	0.82[b]
Age at diagnosis (y), median (IQR)	64 (60, 68)	61 (53, 66)	65 (63,68)	64 (60, 68)	57 (55, 60)	0.07[a]
Maximum PSA level at diagnosis (ng/mL), median (IQR)	7.9 (5.6, 12)	8.2 (6, 11)	9.8 (7.4, 13)	7.5 (5.6, 12)	12.1 (8.5, 13)	0.78[a]
Post-RP Gleason Sum Score (GSS), median (IQR)	7 (7,7)	7 (7. 8)	7 (6,7)	7 (7,7)	6 (6, 7)	0.08[b]
High-risk Prognostic stage grouping, %	58.6	71.4	60	59	40	0.75[b]

[a]Kruskal-Wallis One Way Analysis of Variance on Ranks, [b]Fisher test

Post-RP histology

Percentage of patients recording extra-prostatic extension (EPE), seminal vesicle invasion (SVI) and positive surgical margins (PSM), peri-neural invasion (PNI) and lymph node invasion (LNI) compared to world averages are given in **Table 2**.

Table 2. Histology characteristics of the RP sub-cohort compared to reference world averages.

		Prioritised Ethnicity*				
Variable	All	Maori	Pacific-Peoples	NZ-European	Others	reference world averages
EPE %	39	29	40	39	40	19-30 [(4, 5)]
SVI %	16	29	40	15	0	5-6.1 [(5, 6)]
PNI %	66	71	60	65	80	78-90 [(4, 7)]
PSM %	44	43	40	45	20	15-26 [(5, 6)]
LNI %	3	0	0	3.4	0	0.9-2.5 [(6, 7)]

Age and maximum PSA level at diagnosis, prostate weight, PSAD, and post-RP GSS, were not significantly different between ethnic groups (**Figs. 1 and 2**). The MTD was significantly higher among Māori patients compared to other ethnic groups **(Fig.1; *p*=0.01).** Māori men were diagnosed at a younger median age compared to Pacific and European men (**Fig.1)** and with a higher proportion of men with GSS of 8 & 9 **(Fig.2)** compared to other ethnic groups, although these differences were not statistically significant.

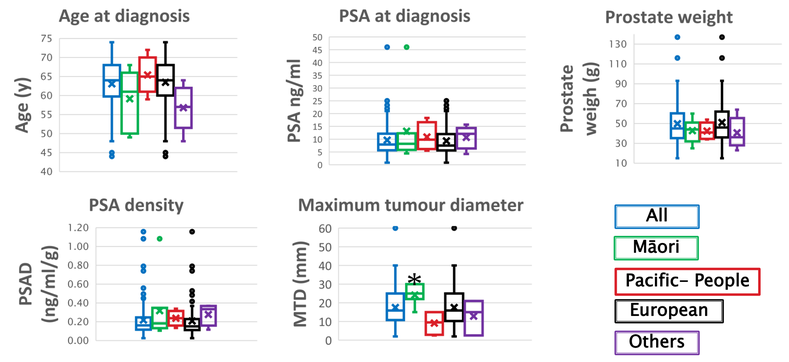

Figure 1. Maximum PSA level at diagnosis, prostate weight, PSA density (PSAD), age at diagnosis, and maximum tumour diameter (MTD) in the overall cohort and across prioritized ethnic groups. Box plots display median (line within box) and quartiles (box limits), mean (x), range (whiskers) and outliers. * = Māori men recorded the highest significant MTD median of 25.0mm (IQR: 22.0, 27.5) compared to other ethnic groups (*p*=0.01).

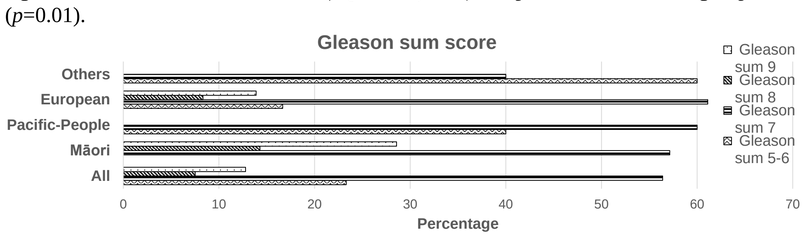

Figure 2. Gleason sum score distributions with and without stratification by prioritized ethnicities.

Subsequent treatments recorded by 2013

In this RP-sub-cohort, 22.4% were treated with adjuvant or salvage therapy after a median follow-up of 3.4 years (IQR: 2.1, 5.4). The highest proportion (71.4%) of these treatments were performed on those recording SVI. Overall, 26.7% were treated with radiation therapy (RT), 50% with androgen deprivation therapy (ADT) and 23.3% with both RT and ADT. The proportion of men receiving both RT and ADT were highest among those with SVI (33.3%) and this increased further to 41.7% if they also recorded EPE or PSM (**Table 4**). Post-RP treatments of RT, or ADT, or both were received by 6.8%, 11.1%, and 5.9% of European cases, while 28.6% of Māori cases received ADT. No post-RP treatments were received by Pacific-People and 'Others' ethnic group.

Table 4. Histology status and subsequent treatments with RT or ADT or both.

		Subsequent treatments n, (%)	RT n, (%)	ADT n, (%)	RT+ADT n, (%)
EPE	Yes (n=52)	20 (38.5)	4 (20)	11 (55)	5 (25)
	No (n=82)	9 (11.0)	4 (44.4)	3 (33.3)	2 (22.2)
SVI	Yes (n=21)	15 (71.4)	2 (13.3)	8 (53.3)	5 (33.3)
	No (n=113)	15 (13.3)	6 (40.0)	7 (46.7)	2 (13.3)
PNI	Yes (n=88)	24 (27.3)	7 (29.2)	11 (45.8)	6 (25.0)
	No (n=46)	6 (13.0)	1 (16.7)	4 (66.7)	1 (16.7)
PSM	Yes (n=59)	19 (32.2)	4 (21.1)	9 (47.4)	6 (31.6)
	No (n=75)	7 (9.3)	1 (14.3)	5 (71.4)	1 (14.3)
LNI	Yes (n=4)	4 (100)	-	3 (75.0)	1 (25.0)
	No (n=130)	26 (20)	8 (30.8)	12 (46.2)	6 (23.1)
EPE+SVI	Yes (n=16)	12 (75)	1 (8.3)	6 (50.0)	5 (41.7)
PNI+SVI	Yes (n=19)	14 (73.7)	2 (14.3)	7 (50.0)	5 (35.7)
PSM+SVI	Yes (n=17)	12 (70.6)	1 (8.3)	6 (50.0)	5 (41.7)
LNI+SVI	Yes (n=3)	3 (100)	0	2 (66.7)	1 (33.3)
Total		30 (22.4)	8 (26.7)	15 (50.0)	7 (23.3)

Mortality and survival

Overall mortality of this cohort during the assessment period was 16.4% while in Māori men this was 28.6%. Overall prostate-cancer specific mortality (PCSM) was 4.5% while the highest was recorded in Pacific-People (20%) and Europeans recording 4.3%. Māori and 'Other' ethnicities recorded no PCSM during this period. Five year survival was over 96.6% across all ethnicities, while median survival was not significantly different among ethnicities (**Table 5**).

Table 5. Mortality and survival rates with and without stratification by ethnicity.

		Maori	Pacific-People	European	Others	Overall
All Cause mortality n (%)	Yes	2 (28.6)	1 (20)	19 (16.2)	0 (0)	22 (16.4)
	No	5 (71.4)	4 (80)	98 (83.8)	5 (100)	112 (83.6)
PC-specific mortality n (%)	Yes	0 (0)	1 (20)	5 (4.3)	0 (0)	6 (4.5)
	No	7 (100)	4 (80)	112 (95.7)	5 (100)	128 (95.5)
Five-year survival n (%)		7 (100)	5 (100)	113 (96.6)	5 (100)	130 (97%)
Median survival in y, median, IQR		7.6 (5.7, 10.7)	8.6 (7.8,10.8)	8.3 (7.1, 10.8)	9.3 (7.6, 9.7)	8.3 (7.1, 10.6)
		P value[a] = 0.883				

[a]Kruskal-Wallis One Way Analysis of Variance on Ranks

Diagnosis precision

Data indicates an overall PC under-diagnosis rate of 62% while in Māori men this is much higher reaching up to 71.4% (**Fig.3**). Previous recorded under-diagnosis rates have ranged from 18.6% - 42.2%[3]. Overall over-diagnosis rate of 8.2% is much lower than the world records of 20-67%[9,10].

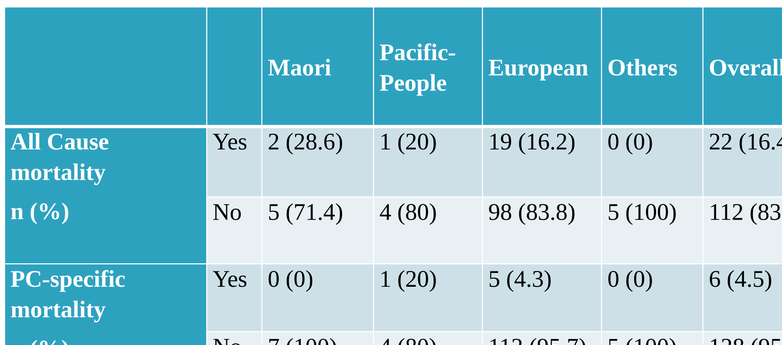

Figure 3. Percentages of over-, under- and accepted diagnoses of PC with and without stratification by ethnicities.

Discussion

Higher percentages of patients recording EPE, SVI and PSM as well as higher PSAD compared to world averages are a concern as such factors are reported to have associations with biochemical recurrence (BCR) of disease post-surgery[4,5,7]. Although general patient characteristics did not differ significantly between ethnicities, Māori and Pacific-People in particular recorded higher SVI rates with almost two fold in Māori men and >two fold in Pacific men compared to the NZ Europeans. As subsequent adjuvant or salvage therapies were associated with SVI, these higher rates of SVI invariably lead to higher public and social health burdens. MTD was significantly higher in Māori men and could be associated with delayed diagnoses. Pacific men have recorded the highest PCSM (4.4 times the average) although they record lower GSS cancers. Māori men recorded the highest overall mortality rate (1.7 times the average), but with a zero PCSM rate indicating deaths in association with comorbidities. Under-diagnosis rate overall was higher than recorded world averages and has exacerbated in Māori men.

Among the limitations of the current analyses are-

1.The relatively small number of subjects available for analyses, especially Māori and Pacific-People. Therefore, interpretations should be made with caution.

2. Lack of parallel BCR data for this analysis, limits the understanding of post-RP management status >8y since RP. However, this is partially compensated by adjuvant and salvage therapies recorded up to 2013 (3.4y ([QR: 2.1, 5.4] since RP) and mortality and survival outcomes recorded at 8.4y.

Extended analyses with patients from other regions of NZ as well as more Māori and Pacific men may provide better understanding of the status of PC outcomes in men managed with RP in NZ.

References

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