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Original Article

Risk of Under-treatment and Over-treatment in a Group of Australian Men Diagnosed with Prostate Cancer

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Abstract

Background and objectives: Patients with newly diagnosed prostate cancer (PCA) face the critical decision of whether to undergo treatment with curative intent (TCI, surgery or radiation) or conservative treatment on the background of a cancer where the potential for over-treatment and under-treatment is real. This study aimed to investigate the influence of cancer- and patient-related factors on the initial treatment decision for men with a new diagnosis of PCA and to evaluate treatment decisions against relevant guidelines.

Methods: This study undertook a retrospective audit of the clinical records of 545 men who were diagnosed with PCA at four Australian urology services. Age, comorbidities, and cancer-related factors were recorded, with patients divided into risk groups based on cancer factors.

Results: Cancer risk stratification emerged as a primary determinant influencing individual treatment choices, with low-risk patients being more likely to have active surveillance and those classified as intermediate or high-risk being more likely to have TCI. Surgery was more commonly offered to younger patients and those with fewer comorbidities. While 80% of patients received guideline-concordant treatment, 20% were identified as being over-treated, receiving TCI despite limited life expectancy and/or high comorbidities.

Conclusions: Managing men diagnosed with PCA should avoid under-treatment in young, otherwise healthy individuals with aggressive cancer by offering TCI. Conversely, over-treatment (unnecessary treatment), especially in men with low-grade cancer or individuals with limited life expectancy due to significant comorbidities, should be avoided to prevent unnecessary treatment when competing causes are more likely to be fatal than prostate cancer.

Introduction

Each year, approximately 17,000 Australian men diagnosed with prostate cancer (PCA) face a difficult decision whether to undergo treatment.[1] This decision is difficult due to uncertainty about the risk of progression of cancer (and therefore the need for treatment), as well as the limited proven efficacy of PCA treatments in improving survival.[2–4] Further complicating matters include the moderate risk of treatment-related side-effects impacting bladder, bowel and sexual function, potentially leading to adverse effects on physical, psychological and sexual well-being.[5] Consequently, patients newly diagnosed with PCA are compelled to consider treatment options at a time of high psychological stress.[6] Decision-making may therefore be significantly influenced by the patient's preferences, which may be based on anxiety, fear, and the personal stories of family and other men, as well as more factual analysis, and possible cognitive decline.[7]

Patients diagnosed with PCA can undergo treatment with curative intent (TCI) with either surgery or radiation therapy, or treatment with non-curative intent (TNCI) including active surveillance, watchful waiting, or androgen deprivation therapy.[8] The aim of managing PCA is to strike a balance, avoiding both under-treatment and over-treatment.[9] Exact definitions of these terms are difficult and controversial,[10] but Loeb *et al* suggest that

Keywords: Prostate cancer; Risk stratification; Screening; Treatment decision making; Under-treatment; Over-treatment; Clinical guidelines; Comorbidity.

Abbreviations: ADT, androgen deprivation therapy; ASTRO, the American Society for Radiation Oncology; AUA, American Urological Association; CCI, Charlson comorbidity index; DRE, Digital rectal examination; PCA, prostate cancer; PSA, prostate specific antigen; TCI, treatment with curative intent; TNCI, treatment with non-curative intent.

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Table 1. Classification of patients into AUA/ASTRO Risk groups and the Lunardi *et al* algorithm to determine under- or over-treatment[23]

	D'Amico risk group	PCA grade group	PSA (ng/mL)	Clinical stage	Recommended treatment
(a) AUA/ASTRO risk groups					
Low-Risk	Low	1	<10	T1-T2a	AS
Intermediate-Favourable	Intermediate	1	10 to <20	≤T2b-c	AS or TCI
	Intermediate	2	<10	≤T2b-c	AS or TCI
Intermediate-Unfavourable	Intermediate	2	10 to <20	≤T2b-c	TCI or WW
	Intermediate	3	<20	≤T2b-c	TCI or WW
High-Risk	High	4 or 5	≥20	≥T3	TCI or WW
(b) Determination of under- or over-treatment (Lunardi et al algorithm)[26]					
Treatment	D'Amico risk group	Age	CCI	Over-treatment	Under-treatment
TCI	any	<75	≥2	✓	
TCI	any	>75	≥1	✓	
TCI	Low	65–75	≤1	✓	
None	Intermediate/ high	<75	≤1		✓
None	Intermediate/ high	75–85	0		✓

PCA, prostate cancer, PSA, prostate specific antigen, AS, active surveillance, WW, watchful waiting, TCI, (Treatment with curative intent) with either surgery or radiation therapy, CCI Charlson Comorbidity Index.

over-treatment occurs when TCI is applied to a cancer detected through screening and that would not have been detected clinically or symptomatically in the patient's lifetime.[9]

The imperative, therefore, is to identify and treat men with aggressive PCA who have a long life expectancy, thus avoiding under-treatment in these men.[3] Moreover, clinicians must avoid over-treatment in men with limited life expectancy due to age, those with comorbidities who are likely to die from other causes, and those who have low-grade cancer and are therefore at low risk of PCA progression.[11,12] Generally, younger men, with longer life expectancy and aggressive cancer have been shown to benefit significantly from TCI. However, there are also older otherwise healthy men with more aggressive cancers who may benefit from TCI but do not receive it.[13–16]

This study aimed to investigate the influence of cancer-related factors and patient-related factors (age and comorbidities) on the initial treatment decision for men with a new diagnosis of PCA. Treatment decisions were subsequently evaluated for alignment with the relevant guidelines and possible under- or over-treatment identified. This study is important as treating physicians need to carefully consider both cancer and patient factors when making treatment decisions if they are to avoid under- or over-treatment.

Methods and methods

The clinical records of 545 men who underwent prostate biopsy at four Australian-based urology services between January 2015 and December 2016 and received a first diagnosis of PCA were audited for this study. Two practices are located in metropolitan areas (n = 109 patients, two urologists), one in rural NSW (n = 99 patients, two urologists) and one in regional NSW (n = 337 patients, five urologists). The study was approved by the local Human Research Ethics Committee (HREC approval 2016/955).

Treatment

Patients were classified according to the treatment they underwent following their diagnosis of PCA. Patients allocated to the TCI group received surgery or radiation therapy. In this study, surgery refers to radical prostatectomy, either open or robotic-assisted.[17] Radiation therapy refers to treatment with interstitial seeds (brachytherapy) or external beam radiation.

Patients in the TNCI group were allocated to receive active surveillance, watchful waiting, or androgen deprivation therapy (ADT).

Patient related factors

As part of the audit, patient demographic factors such as age, Charlson Comorbidity Index (CCI) and number of medications were recorded.[18,19] Patient age was used to determine overall life expectancy based on the Australian Bureau of Statistics (ABS) life tables.[20] The CCI was chosen because it is a validated tool for assessing comorbidities and is a strong predictor of overall survival and life expectancy.[10,18] Additionally, the patients' medical records were examined, and the number of regular medications prescribed was recorded as a numerical value.

Cancer related factors

Pathological details including serum prostate specific antigen (PSA) levels, cancer stage and tumor grade were collected from the prostate biopsy reports in the patients' medical records. The clinical stage (using the 1992 American Joint Commission on Cancer (AJCC) staging system) was obtained either from the Digital Rectal Examination (DRE) findings recorded in the patient's file or from the DRE findings recorded at the time of biopsy.[21] The D'Amico risk group incorporates PSA, grade and clinical stage and guides to disease severity and prognosis.[22] These risk groups correlate with biochemical recurrence, cancer specific survival and overall survival.[23,24] Patients were classified into four risk groups according to the American Urological Association (AUA) and the American Society for Radiation Oncology (ASTRO) based on these D'Amico risk groups (Table 1a).[23,25,26] Treatments received by patients in this study were compared with these guidelines to

Table 2. Audit of the factors affecting patient treatment choices following a diagnosis of PCA

	Total	Low risk	Intermediate favorable	Intermediate unfavorable	High risk
n (%)	545	111 (20.4%)	148 (27.2%)	120 (22%)	166 (30.4%)
Age (years, mean)	67.5	63.1	66.7	68.9	70.3
Average CCI	0.63	0.55	0.51	0.57	0.85
Number of medications	2.9	2.5	2.8	2.7	3.3
Median PSA	8	5.6	6.9	9.5	12
Treatment with Curative Intent (TCI)					
Total	347 (63.7%)	29 (26.1%)	114 (77%)	89 (74.2%)	116 (69.9%)
Surgery n (%)	213 (39%)	22 (19.8%)	81 (54.7%)	59 (49.2%)	51 (30.7%)
Radiation n (%)	134 (24.6%)	7 (6.3%)	32 (21.6%)	30 (25%)	65 (39.2%)
Treatment with non-curative intent (TNCI)					
Total	198 (36.3%)	82 (73.9%)	35 (23%)	31 (25.8%)	50 (30.1%)
Watchful waiting n (%)	63 (11.6%)	8 (7.2%)	22 (14.9%)	22 (18.3%)	11 (6.6%)
Active surveillance n (%)	88 (16.1%)	74 (66.7%)	10 (6.8%)	4 (3.3%)	0 (0%)
ADT n (%)	47 (8.6%)	0 (0%)	3 (2%)	5 (4.2%)	39 (23.5%)
Concordance with recommended treatments					
Concordance n (%)	440 (80%)	74 (66.7%)	123 (83.1%)	89 (74.2%)	154 (94%)
Non-concordance n (%)	104 (19%)	37 (33.3%)	25 (16.9%)	31 (25.8%)	11 (6.6%)
Non-Concordance, treated with Surgery	22 (19.8%)	22 (19.8%)	0	0	0
Non-Concordance, No treatment	67 (64%)	8 (7.2%)	22 (14.9%)	26 (21.7%)	11 (6.6%)
Non-Concordance, Life expectancy <10 yrs	15	0	4	8	3
Lunardi estimate of over or under-treatment					
Over-treatment n (%)	77 (14%)	10 (9%)	22 (14.9%)	15 (12.5%)	30 (18.1%)
Under-treatment n (%)	45 (8.3%)	0 (0%)	27 (18%)	14 (12%)	4 (2.4%)

ADT, androgen deprivation therapy; CCI, Charlson comorbidity index; PSA, prostate specific antigen; TCI, Treatment with Curative Intent; TNCI, Treatment with non-curative intent.

determine concordance.

Lunardi *et al*.[26] have developed an algorithm which considers both patient related factors (age and CCI) and cancer-related factors (D'Amico risk group) to determine under- or over-treatment of men with PCA (Table 1b).

Statistical analysis

Descriptive statistics were used to provide an overview of the respondents' sociodemographic characteristics. To determine if the differences between the two groups were significant, when one value (the independent variable) was categorical, and the other was numerical or non-parametric (not normally distributed), the Mann-Whitney test was used as there were two categorical groups. When one value was numerical (and normally distributed) and the other was categorical, an unpaired *t* test was performed if there were two categorical groups. All analyses were performed using Prism 7 for MacOSX (GraphPad Software Inc.). Significance was set at a level of $p < 0.05$.

Results

The average age of the 545 patients included in this study was 67.5 years, with a range of 44 to 91 years (Table 2). The median PSA concentration was 8.0 ng/mL, ranging from 5.6 ng/mL in the Low-Risk group to 12 ng/mL in the High-Risk group. The average CCI for the entire cohort was 0.63, and the average number of medications was 2.9. Over 63.7% of the patients underwent TCI, and two-thirds of those underwent surgery. The percentage of patients receiving TCI did not vary based on geographical location ($p = 0.709$, Chi Square with Fisher's exact test). Surgery was equally available in each of the practice settings. Specifically, surgery was chosen as the treatment option by 24% of patients from the metropolitan settings, 45% of patients in the regional settings and 34% of patients in the rural settings.

The distribution of patients across the four risk categories is detailed in Table 2. The AUA/ASTRO risk stratification was shown to be a primary determinant of treatment options for individual patients, with Low-Risk patients being more likely to have active surveillance and patients classified as Intermediate (Favorable and Unfavorable) or High-Risk being more likely to have TCI (surgery or radiation) (Fig. 1).

Treatment decisions for patients across all risk groups

Younger patients were more likely to be offered surgery (mean

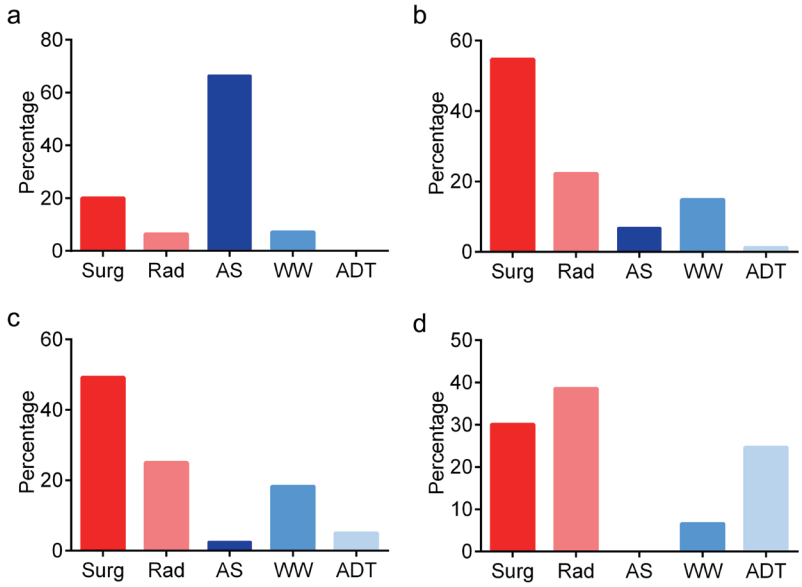

Fig. 1. PCA treatment according to the AUA/ASTRO risk classification. TCI, surgery (Surg) radiation therapy (Rad) is compared with TNCI active surveillance (AS), watchful waiting (WW) and androgen deprivation therapy (ADT) for each of the AUA/AUSTRO risk categories: Low risk (a), intermediate favorable (b), intermediate unfavorable (c) and high risk (d). ADT, androgen deprivation therapy; AS, active surveillance; AUA/ASTRO, American Urological Association/the American Society for Radiation Oncology; PCA, prostate cancer; Rad, radiation therapy; Surg, surgery; TNCI, treatment with non-curative intent; WW, watchful waiting.

age 64.3 years) or active surveillance (mean age 61.8 years), and older patients were more likely to be treated with radiation, watchful waiting, or ADT. Patients treated with surgery were younger (mean age: 64.3 years) than those treated with all other treatment options combined (mean age: 69.7 years, $p < 0.0001$). Patients treated with surgery also had a significantly lower CCI (mean: 0.64) than all the other patients combined (mean CCI: 0.96, $p < 0.0026$) and were on fewer medications (mean number of medications 2.3) than were all the other patients combined (mean number of medications 3.6, $p < 0.0001$). However, overall, there was no significant difference in the age of patients receiving TCI compared to those receiving TNCI (Fig. 2a). Patients with more comorbidities (as indicated by a higher CCI) were more likely to receive TNCI (Fig. 2b, $p = 0.0018$). Similarly, patients on more medications were more likely to receive TNCI ($P = 0.0442$, Fig. 2c).

Treatment decisions according to the AUA/ ASTRO risk classification

As shown in Figure 1, patients classified as Low-Risk were most likely to undergo active surveillance (66.7% of this group, Table 2), which is in concordance with the AUA/ASTRO guidelines (Table 1a). Most patients who received a treatment not aligned with the AUA/ASTRO guidelines opted for surgery as a TCI option. Taking the Lunardi *et al* algorithm into consideration, 10% of our study population in the Low-Risk group received over-treatment (Table 2).[26] However, all the patients, who received TCI (surgery or radiation) had a life expectancy of >10 years. Among patients classified as Low-Risk, there was no significant difference in age between those who received TCI (mean age 62 years) and those who received TNCI (mean age 63.5 years). Patients who received surgery had significantly lower CCI scores (mean 0.27) than those receiving active surveillance (mean 1.0, $p < 0.0001$).

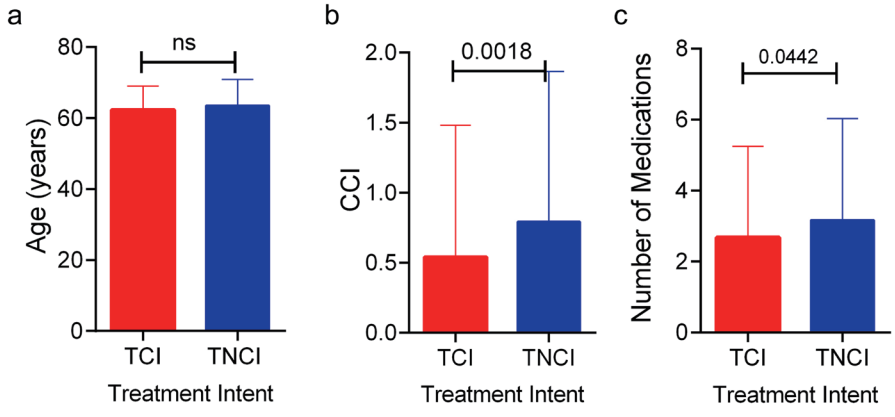

Fig. 2. Influence of patient factors including age (a), co-morbidities (b), as indicated by the CCI and number of medications (c) on treatment intent. CCI, charlson comorbidity index; TCI, treatment with curative intent; TNCI, treatment with non-curative intent.

Overall, 77% of the patients in the Intermediate-Favourable risk group were given TCI (55% surgery, 22% radiation therapy) (Table 2). Patients who received surgery were younger than those who received radiation therapy (mean age: 64 years for surgery versus 71 years for radiation, $p < 0.0001$), and those who received TCI were younger (mean age 66 years) than those who received TNCI (mean age 69 years, $p = 0.0285$, Fig. 3b). Patients who received TNCI were taking significantly more medications (mean 3.7) than those who received TCI (mean 2.5, $p = 0.0288$). Patients treated with surgery also had a lower average CCI (0.33) than those who received radiation therapy (0.87, $p = 0.0350$). However, overall, there was no significant difference in the mean CCI between those receiving TCI and TNCI. The AUA/ASTRO guidelines suggest the use of either the TNCI or the TCI for patients in the Intermediate-Favorable risk group (Table 1a), and there was high concordance in this group (83%, Table 2). According to the Lunardi *et al* algorithm, 15% of patients in this Intermediate-Favorable risk group were judged to have been overtreated either due to a high CCI or being over 75 years of age and still receiving TCI.[26] In this group, 18% of patients (n = 27) were potentially undertreated.

Three-quarters of the patients in the Intermediate-Unfavorable risk group underwent TCI, with almost 50% receiving surgery and an additional 25% receiving radiation therapy (Fig. 1c). Similar to the previous risk group, patients who underwent surgery were younger (mean age 66 years) than those treated with radiation therapy (mean age 72 years, $p = 0.0027$). Those treated with TCI were younger (mean age 67.5 years) than those in the TNCI group (mean age 72.8 years), $p = 0.0007$, Fig. 3c). Those receiving TCI were taking fewer medications (mean 2.4) than those receiving TNCI (mean 3.6, $p = 0.0128$). Likewise, patients who received TCI had a lower CCI (mean 0.5) than those receiving TNCI (mean 0.9, $p = 0.0145$) and those undergoing surgery had a lower CCI (mean 0.3) than those receiving radiation (mean CCI 0.7, $p = 0.0011$) or watchful waiting (mean CCI 1.0, $p < 0.0001$). The AUA/ASTRO guidelines suggest the use of TCI for this group or TNCI if life expectancy is less than 5 years (Table 1a). Overall, three-quarters of patients received treatment in accordance with the guidelines (Table 2). According to the Lunardi *et al* algorithm, 12% of the patients (n = 14) in this risk group were undertreated, and 12.5% patients (n = 15) were considered overtreated because they received TCI despite having a high CCI score or being 75 years and older.[26]

Of the patients in the High-Risk group, 70% (n = 116) received TCI (31% surgery, 39% radiation) (Fig. 1d). Age influenced the treatment received, with patients receiving TCI being younger (average age 68.9 years) than those receiving TNCI (average age 73.7 years, Fig. 3d, $p = 0.0032$). Like patients in the intermediate risk groups, patients who underwent surgery were significantly younger (mean age 65 years) than those receiving radiation therapy (mean age 72 years, $p < 0.0001$). Patients who underwent surgery took fewer medications (mean 2.4) than those treated with radiation (mean 3.9, $p = 0.0136$).

The AUA/ASTRO guidelines suggest TCI or TNCI (watchful waiting) if the life expectancy is less than 5 years for patients classified as High-Risk (Table 1a). The treatment received by 94% of the patients in this High-Risk group was concordant with the guidelines (Table 2). According to the Lunardi *et al* algorithm, 18% of patients were potentially overtreated (Table 1b).

Discussion

The results of our study demonstrated that 80% of patients treated by the participating urologists received appropriate treatment

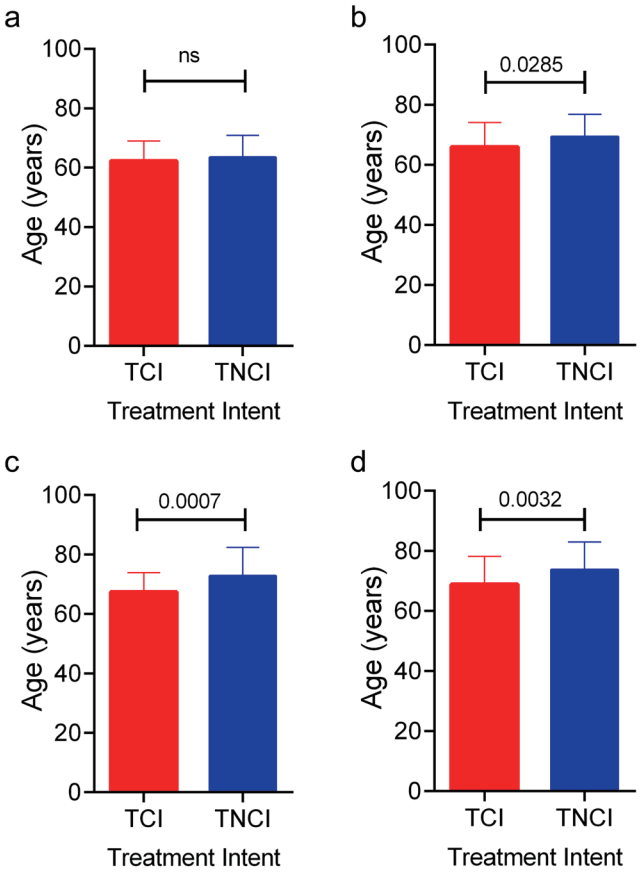

Fig. 3. Effect of age on treatment choice in patients classified as low risk (a), Intermediate Favorable risk (b), Intermediate Unfavorable risk (c) and High Risk (d). TCI, treatment with curative intent; TNCI, treatment with non-curative intent.

based on the AUA/ASTRO guidelines. However, approximately one-third of patients classified as low-risk were not treated in accordance with the guidelines.[25,27] Similar to the findings of the current study, a Victorian prostate cancer registry study, reported by Wang *et al*, showed a correlation between cancer risk stratification and treatment options.[28] In their study, 55% of the low-risk patients received active surveillance, compared to 66% of the patients in our cohort. The most recent report of the Prostate Cancer Outcomes Registry of Australia and New Zealand which included more than 10,000 men diagnosed between 2015 and 2017, showed that, identical to our study, 66% of men with low-risk diseases were diagnosed via observation.[29] In that study, 85% of men in the intermediate risk group received TCI compared to approximately 75% in our study. Our patient group had similar demographics to those in both of these studies. In particular, the risk stratification distribution was similar, suggesting that our patient cohort is representative of Australian patients with PCA in general.[28,29] The results of these studies and ours confirm that patients' treatment options are initially being appropriately influenced by cancer factors.

Once treatment options are established based on cancer factors, patient age, and comorbidities, these factors will modify the available options.[8,30] Across all risk groups, in our study, younger and healthier patients were more likely to undergo TCI, indicating that invasive treatments were given to those most likely to benefit. In the current study, patients classified in the Low-Risk group receiv-

ing TCI had fewer comorbidities than those receiving TNCI. Similarly, for patients classified into the High-Risk group, those receiving surgery were on fewer medications than those receiving other therapies, including radiation (a second TCI). These findings concur with an Australian population-based study of men with a new diagnosis of PCA, which showed that men who were younger (<60 years old) and had fewer comorbidities were more likely to receive surgery (radical prostatectomy).[31] Hence, it is critical to estimate the risk of death from PCA and compare it with the risk to the risk of death from other causes to avoid utilizing TCI in men with limited life expectancy or significant comorbidities.[32] Schymura *et al*.'s study supports this paradigm of treatment with TNCI associated with increasing age, high PSA, low grade cancer and high comorbidity.[33]

Under-treatment should be avoided for men who are young, otherwise healthy, and have aggressive cancer by offering TCI. Similarly, over-treatment (unnecessary treatment) should be avoided in patients with low-grade cancer, or who are likely to die from competing causes, rather than from PCA because of limited life expectancy due to significant comorbidities. However, older, otherwise healthy men with aggressive cancer may need to receive treatment.[29] In our study, over-treatment was identified in 15% of patients, which is slightly lower than the over-treatment rate of 25% reported by Lunardi *et al*.[26] In the current study, like in the Lunardi study, patients identified as being over-treated received TCI despite having a limited life expectancy and/or high incidence of comorbidities. Daskivich *et al*.'s study of nearly 1,500 patients with newly diagnosed low/intermediate risk PCA showed that the risk of death from PCA over 10 years was between 5- and 8% (regardless of the treatment chosen), with 25% of men dying from non-PCA causes.[10] Therefore, for many men, the risk of dying directly from PCA is low, while those with a CCI greater than or equal to 2 have a >75% risk of dying from any cause over 10 years.[3,27] Ultimately, comorbidities have a significant impact on survival, according to Frendl's study showing that age at diagnosis, CCI score, self-reported general health and smoking are the most predictive risk factors for mortality.[14] Scores utilizing medication use have been shown to be a good measure of comorbidity.[34,35]

The impact of age on treatment choice following a diagnosis of PCA is complex. Research has established that older individuals, males, and those with lower education levels are more likely to prefer a more passive role in treatment decisions, potentially hindering their full participation in the decision-making process.[36] This could affect many men with prostate cancer. Moreover, increasing age has been associated with the tendency to seek less information, make decisions more quickly, prefer fewer options, have increased difficulty understanding information, and place greater emphasis on emotional aspects when making decisions.[37] In addition, some patients wish to avoid having to make choices and therefore rate physician advice as the most important factor in treatment decision-making.[38,39] Importantly, some physicians maintain a paternalistic view of decision making and may not fully explore the patients' wishes,[40] despite the evidence suggesting that greater patient involvement in the decision-making process leads to increased patient satisfaction with the decision.[41,42]

Age is a significant independent risk factor for comorbidities and plays a pivotal role in determining treatment options.[12] In our study, patients receiving TCI were significantly younger than those choosing TNCI for the Intermediate-Favorable, Intermediate-Unfavorable and High-Risk groups. Clinicians can use ABS life tables as a crude estimate of life expectancy based on age.[43] However, these tables do not consider health status or comorbidities and have been shown to overestimate life expectancy significantly, especially in older men, which may contribute to possible overtreatment.[11,12] Despite this evidence, Daskivich *et al*. suggested that clinicians tend to emphasize age (and crude estimates of life expectancy) over comorbidities when making treatment decisions.[10] Hoffman *et al*. confirmed that comorbidity is a more significant determinant of life expectancy than age.[11,16]

However, until recently, the focus of the discussion has been on over-treatment of older men with co-morbidities. It is crucial to recognize that some older men with aggressive cancer may be unjustly denied TCI based merely on their age, and thus suffer from undertreatment. For older men with high grade disease, the lethality of PCA should not be underestimated, especially for those with fewer comorbidities.[16] In our study, 12–18% of men in the intermediate risk groups did not receive TCI despite having no comorbidities suggesting possible undertreatment of this group of men. Lu-Yao showed that men with high-risk diseases and a life expectancy greater than 10 years face a significant risk (>25%) of PCA specific mortality within that 10-year period, suggesting the potential benefits of active treatment.[13] However, men over 70 years are less likely to receive TCI, regardless of cancer grade or CCI, suggesting that age alone, rather than cancer grade or comorbidities, is the prime determinant of treatment options for these individuals.[36] In Frendl *et al*'s study, for men over 65 years, only 40% of those who died due to PCA had undergone definitive treatment, indicating potential undertreatment in this older age group.[14]

Conclusions

The aim in treating men diagnosed with PCA should be to avoid under-treatment in men who are young, healthy, and have aggressive cancer by offering TCI. Conversely, over-treatment or unnecessary treatment should be avoided in men with low-grade cancer or in those who are likely to die from competing causes rather than from PCA because of limited life expectancy or significant comorbidities. The results of the current study demonstrated that 80% of patients treated by the participating urologists received appropriate treatment according to the AUA/ASTRO guidelines. Ultimately cancer factors are the prime determinants of treatment options and can be modified by life expectancy and comorbidities. Physicians must be careful not to overestimate the lethality of cancer and underestimate the potential for age and comorbidities to be more likely causes of death while still offering TCI to those most likely to benefit.

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Conflict of interest

The authors have no conflict of interests related to this publication.

Author contributions

Study concept and design (TAS, JRM, KJM), acquisition of data

(TAS, WW, SN), analysis and interpretation of data (TAS, WW, SN, KJM), drafting of the manuscript (TAS, JRM, KJM), critical revision of the manuscript for important intellectual content (JRM, KJM) and study supervision (KJM). All authors have made a significant contribution to this study and have approved the final manuscript.

Data sharing statement

The complied audit data used to support the findings of this study are included within the article; The data relating to individual patients used to support the findings of this study have not been made available because of restrictions associated with ethics approval.

Ethical statement

This study was approved by the Joint University of Wollongong/Illawarra Shoalhaven Local Health District Human Research Ethics Committee (HREC approval 2016/955). The study conformed with the ethical guidelines of the Helsinki Declaration (as revised in 2013). As this study was an audit of clinical notes, approval from each individual patient was not required.

References

[1] Australian Government, Cancer Australia. Prostate Cancer in Australia Statistics [Internet]. Canberra: Australian Government, Cancer Australia, 2021. [Cited 2021 October 17]. Available from: https://www.canceraustralia.gov.au/cancer-types/prostate-cancer/statistics.

[2] Hamdy FC, Donovan JL, Lane JA, Mason M, Metcalfe C, Holding P, *et al*. 10-Year Outcomes after Monitoring, Surgery, or Radiotherapy for Localized Prostate Cancer. N Engl J Med 2016;375(15):1415–1424. doi:10.1056/NEJMoa1606220, PMID:27626136.

[3] Wilt TJ, Jones KM, Barry MJ, Andriole GL, Culkin D, Wheeler T, *et al*. Follow-up of Prostatectomy versus Observation for Early Prostate Cancer. N Engl J Med 2017;377(2):132–142. doi:10.1056/NEJMoa1615869, PMID:28700844.

[4] Daskivich TJ. Life expectancy and treatment choices for men with high-risk prostate cancer. Eur Urol 2015;68(1):59–60. doi:10.1016/j.eururo.2015.01.006.

[5] Mazariego CG, Egger S, King MT, Juraskova I, Woo H, Berry M, *et al*. Fifteen year quality of life outcomes in men with localised prostate cancer: population based Australian prospective study. BMJ 2020;371:m3503. doi:10.1136/bmj.m3503, PMID:33028540.

[6] Steginga SK, Occhipinti S, Gardiner RA, Yaxley J, Heathcote P. Prospective study of men's psychological and decision-related adjustment after treatment for localized prostate cancer. Urology 2004;63(4):751–756. doi:10.1016/j.urology.2003.11.017, PMID:15072894.

[7] Berry DL, Ellis WJ, Russell KJ, Blasko JC, Bush N, Blumenstein B, *et al*. Factors that predict treatment choice and satisfaction with the decision in men with localized prostate cancer. Clin Genitourin Cancer 2006;5(3):219–226. doi:10.3816/CGC.2006.n.040, PMID:17239276.

[8] Mottet N, Bellmunt J, Bolla M, Briers E, Cumberbatch MG, De Santis M, *et al*. EAU-ESTRO-SIOG Guidelines on Prostate Cancer. Part 1: Screening, Diagnosis, and Local Treatment with Curative Intent. Eur Urol 2017;71(4):618–629. doi:10.1016/j.eururo.2016.08.003, PMID:27568654.

[9] Loeb S, Bjurlin MA, Nicholson J, Tammela TL, Penson DF, Carter HB, *et al*. Overdiagnosis and overtreatment of prostate cancer. Eur Urol 2014;65(6):1046–1055. doi:10.1016/j.eururo.2013.12.062, PMID:24439788.

[10] Daskivich TJ, Chamie K, Kwan L, Labo J, Dash A, Greenfield S, Litwin MS. Comorbidity and competing risks for mortality in men with prostate cancer. Cancer 2011;117(20):4642–50. doi:10.1002/cncr.26104, PMID:21480201.

[11] Hoffman RM, Koyama T, Albertsen PC, Barry MJ, Daskivich TJ, Goodman M, *et al*. Self-Reported Health Status Predicts Other-Cause Mortality in Men with Localized Prostate Cancer: Results from the Prostate Cancer Outcomes Study. J Gen Intern Med 2015;30(7):924–934. doi:10.1007/s11606-014-3171-8, PMID:25678374.

[12] Walz J, Suardi N, Shariat SF, Jeldres C, Perrotte P, Graefen M, *et al*. Accuracy of life tables in predicting overall survival in patients after radical prostatectomy. BJU Int 2008;102(1):33–38. doi:10.1111/j.1464-410X.2008.07614.x, PMID:18384631.

[13] Lu-Yao GL, Albertsen PC, Moore DF, Shih W, Lin Y, DiPaola RS, *et al*. Outcomes of localized prostate cancer following conservative management. JAMA 2009;302(11):1202–1209. doi:10.1001/jama.2009.1348, PMID:19755699.

[14] Frendl DM, FitzGerald G, Epstein MM, Allison JJ, Sokoloff MH, Ware JE. Predicting the 10-year risk of death from other causes in men with localized prostate cancer using patient-reported factors: Development of a tool. PLoS One 2020;15(12):e0240039. doi:10.1371/journal.pone.0240039, PMID:33284845.

[15] Vickers A, Bennette C, Steineck G, Adami HO, Johansson JE, Bill-Axelson A, *et al*. Individualized estimation of the benefit of radical prostatectomy from the Scandinavian Prostate Cancer Group randomized trial. Eur Urol 2012;62(2):204–209. doi:10.1016/j.eururo.2012.04.024, PMID:22541389.

[16] Hoffman KE. Management of older men with clinically localized prostate cancer: the significance of advanced age and comorbidity. Semin Radiat Oncol 2012;22(4):284–294. doi:10.1016/j.semradonc.2012.05.005.

[17] Scherr D, Swindle PW, Scardino PT. National Cancer Comprehensive Network guidelines for the management of prostate cancer. Urology 2003;61(Suppl 2A):14–24. doi:10.1016/s0090-4295(02)02395-6.

[18] Charlson M, Szatrowski TP, Peterson J, Gold J. Validation of a combined comorbidity index. J Clin Epidemiol 1994;47(11):1245–1251. doi:10.1016/0895-4356(94)90129-5.

[19] Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chron Dis 1987;40(5):373–383. doi:10.1016/0021-9681(87)90171-8.

[20] Australian Bureau of Statistics. Statistics about life tables for Australia, states and territories and life expectancy at birth estimates for sub-state regions [Internet]. Canberra: Australian Bureau of Statistics, 2020. [cited 2020 December 5th]. Available from: https://www.abs.gov.au/statistics/people/population/life-tables/latest-release#data-download.

[21] American Cancer Society. Prostate Cancer. Early detection diagnosis and staging [Internet]. Atlanta, GA: American Cancer Society, 2021. [Cited 24 October 2021]. Available from: https://www.cancer.org/cancer/prostate-cancer/detection-diagnosis-staging/staging.htmL.

[22] Boorjian SA, Karnes RJ, Rangel LJ, Bergstralh EJ, Blute ML. Mayo clinic validation of the D'Amico risk group classification for predicting survival following radical prostatectomy. J Urol 2008;179(4):1354–1361. doi:10.1016/j.juro.2007.11.061.

[23] Tosoian JJ, Chappidi M, Feng Z, Humphreys EB, Han M, Pavlovich CP, *et al*. Prediction of pathological stage based on clinical stage, serum prostate-specific antigen, and biopsy Gleason score: Partin Tables in the contemporary era. BJU Int 2016;119(5):676–683. doi:10.1111/bju.13573.

[24] D'amico AV, Whittington R, Malkowicz SB, Schultz D, Blank K, Broderick GS, *et al*. Biochemical outcome after radical prostatectomy, external beam radiation therapy, or interstitial radiation therapy for clinically localized prostate cancer. JAMA 1998;280(11):969–974. doi:10.1001/jama.280.11.969.

[25] American Urological Association. Clinically Localized Prostate Cancer: AUA/ASTRO/SUO Guideline [Internet]. Linthicum, MA: American Urological Association, 2017. [cited 2021 October 24]. Available from: https://www.auanet.org/guidelines/prostate-cancer-clinically-localized-guideline.

[26] Lunardi P, Ploussard G, Grosclaude P, Roumiguie M, Soulie M, Beauval JB, Malavaud B. Current impact of age and comorbidity assessment on prostate cancer treatment choice and over/undertreatment risk. World J Urol 2016;35(4):587–593. doi:10.1007/s00345-016-1900-9.

[27] Albertsen PC, Moore DF, Shih W, Lin Y, Li H, Lu-Yao GL. Impact of comorbidity on survival among men with localized prostate cancer. J

Clin Oncol 2011;29(10):1335–1341. doi:10.1200/JCO.2010.31.2330, PMID:21357791.
[28] Wang LL, 'Begashaw K, Evans M, Earnest A, Evans SM, Millar JL, *et al*. Patterns of care and outcomes for men diagnosed with prostate cancer in Victoria: an update. ANZ J Surg 2018;88(10):1037–1042. doi:10.1111/ans.14722.
[29] O'Callaghan M, Pase M, Frydenberg M, Mark S, Moretti K, Maqsood S, *et al*. Prostate Cancer in Australian and New Zealand Men, Patterns of care within PCOR-ANZ 2015–2017 [Internet]. Melbourne, VIC: Monash University and Movember, 2019. [Cited 2021 December 14].
[30] Hall WH, Jani AB, Ryu JK, Narayan S, Vijayakumar S. The impact of age and comorbidity on survival outcomes and treatment patterns in prostate cancer. Prostate Cancer Prostatic Dis 2005;8(1):22–30. doi:10.1038/sj.pcan.4500772.
[31] Yap ML, O'Connell DL, Goldsbury DE, Weber MF, Smith DP, Barton MB. Patterns of care for men with prostate cancer: the 45 and Up Study. MJA 2021;214(6):271–278. doi:10.5694/mja2.50966.
[32] Kutikov A, Cooperberg MR, Paciorek AT, Uzzo RG, Carroll PR, Boorjian SA. Evaluating prostate cancer mortality and competing risks of death in patients with localized prostate cancer using a comprehensive nomogram. Prostate Cancer Prostatic Dis 2012;15(4):374–379. doi:10.1038/pcan.2012.21, PMID:22710832.
[33] Schymura MJ, Kahn AR, German RR, Hsieh MC, Cress RD, Finch JL, *et al*. Factors associated with initial treatment and survival for clinically localized prostate cancer: results from the CDC-NPCR Patterns of Care Study (PoC1). BMC Cancer 2010;10:152. doi:10.1186/1471-2407-10-152, PMID:20403178.
[34] Perkins AJ, Kroenke K, Unützer J, Katon W, Williams JW, Hope C, *et al*. Common comorbidity scales were similar in their ability to predict health care costs and mortality. J Clin Epidemiol 2004;57(10):1040–1048. doi:10.1016/j.jclinepi.2004.03.002.
[35] Olthof M, Stevens M, Zijlstra WP, Bulstra SK, van den Akker-Scheek I. Medication use is a better predictor of length of hospital stay in total hip arthroplasty than the American Society of Anesthetists (ASA) Score. J Arthroplasty 2017;32(1):24–27. doi:10.1016/j.arth.2016.06.022.
[36] Lechner S, Herzog W, Boehlen F, Maatouk I, Saum KU, Brenner H, *et al*. Control preferences in treatment decisions among older adults—Results of a large population- based study. J Psychosom Res 2016;86:28–33. doi:10.1016/j.jpsychores.2016.05.004.
[37] van Weert JC, van Munster BC, Sanders R, Spijker R, Hooft L, Jansen J. Decision aids to help older people make health decisions: a systematic review and meta-analysis. BMC Med Inform Decis Mak 2016;16:45. doi:10.1186/s12911-016-0281-8, PMID:27098100.
[38] Fraenkel L, McGraw S. Participation in medical decision making: The patients' perspective. Med Decis Making 2007;27(5):533–538. doi:10.1177/0272989X07306784, PMID:17873253.
[39] Doherr H, Christalle E, Kriston L, Härter M, Scholl I. Use of the 9-item Shared Decision Making Questionnaire (SDM-Q-9 and SDM-Q-Doc) in intervention studies-A systematic review. PLoS One 2017;12(3):e0173904. doi:10.1371/journal.pone.0173904, PMID:28358864.
[40] Gilbert SM, Sanda MG, Dunn RL, Greenfield TK, Hembroff L, Klein E, *et al*. Satisfaction with information used to choose prostate cancer treatment. J Urol 2014;191(5):1265–1271. doi:10.1016/j.juro.2013.12.008, PMID:24333514.
[41] Fischer M, Visser A, Voerman B, Garssen B, van Andel G, Bensing J. Treatment decision making in prostate cancer: patients' participation in complex decisions. Patient Educ Couns 2006;63(3):308–313. doi:10.1016/j.pec.2006.07.009, PMID:16965887.
[42] Nakayama K, Osaka W, Matsubara N, Takeuchi T, Toyoda M, Ohtake N, *et al*. Shared decision making, physicians' explanations, and treatment satisfaction: a cross-sectional survey of prostate cancer patients. BMC Med Inform Decis Mak 2020;20(1):334. doi:10.1186/s12911-020-01355-z, PMID:33317523.
[43] Australian Bureau of Statistics. Life tables. Reference period 2017-2019 [Internet]. Canberra: Australian Bureau of Statistics, 2020. [Cited 2021 October 24]. Available from: https://www.abs.gov.au/statistics/people/population/life-tables/latest-release#data-download.
[44] de Camargo Cancela M, Comber H, Sharp L. Age remains the major predictor of curative treatment non-receipt for localised prostate cancer: a population-based study. Br J Cancer 2013;109(1):272–279. doi:10.1038/bjc.2013.268, PMID:23722470.