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Unstaged cancer in a population-based registry: Prevalence, predictors and patient prognosis

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ABSTRACT

Purpose: Information on cancer stage at diagnosis is critical for population studies investigating cancer care and outcomes. Few studies have examined the factors which impact (1) staging or (2) outcomes for patients who are registered as having unknown stage. This study investigated (1) the prevalence of unknown stage at diagnosis on the New Zealand Cancer Registry (NZCR); (2) explored factors which predict unknown stage; (3) described receipt of surgery and (4) survival outcomes for patients with unknown stage. *Methods*: Patients diagnosed with the most prevalent 18 cancers between 2006 and 2008 ($N = 41,489$) were identified from the NZCR, with additional data obtained from mortality and hospitalisation databases. Logistic and Cox regression were used to investigate predictors of unknown stage and patient outcomes. *Results*: (1) Three distinct groups of cancers were found based on proportion of patients with unknown stage (low = up to 33% unknown stage; moderate = 33–64%; high = 65%+). (2) Increasing age was a significant predictor of unknown stage (adjusted odds ratios [ORs]: 1.18–1.24 per 5-year increase across groups). Patients with substantive comorbidity were more likely to have unknown stage but only for those cancers with a low (OR = 2.65 [2.28–3.09]) or moderate (OR = 1.17 [1.03–1.33]) proportion of patients with unknown stage. (3) Patients with unknown stage were significantly less likely to have received definitive surgery than those with local or regional disease across investigated cancers. (4) Patients with unknown stage had 28-day and 1-year survival which was intermediate between regional and distant disease. *Discussion*: We found that stage completeness differs widely by cancer site. In many cases, the proportion of unknown stage on a population-based register can be explained by patient, service and/or cancer related factors.

1. Introduction

Information on stage (or extent of disease) at diagnosis is critical for studies investigating cancer care and outcomes. Stage at diagnosis is integral to guiding treatment options and to the likelihood of survival from the disease [1,2]. Despite the importance of this information, it is accepted that such data are often missing in population-based cancer registries [2].

Data on stage may be collected by cancer registries directly through synoptic reporting, or more indirectly via registry staff assigning stage using available clinical and pathological data. In New Zealand, registrars manually attribute stage primarily on the basis of pathology reports following tumour excision but also with additional information from hospitalisation records, death certificate and autopsy reports (Fig. 1) [3]. Recent years have seen a shift towards standardised synoptic reporting to cancer registers, with this approach increasingly common in North America and currently under development elsewhere (including in New Zealand) [4,5].

In this study, the term 'unstaged' refers to patients whose stage is recorded as unknown on a population-based cancer dataset or registry. Prevalence of unstaged cancer in this context varies considerably depending on the cancer and population [1,6–15]. Previous studies have generally been limited to investigations of one or a few chosen cancers, with prostate, breast and colorectal

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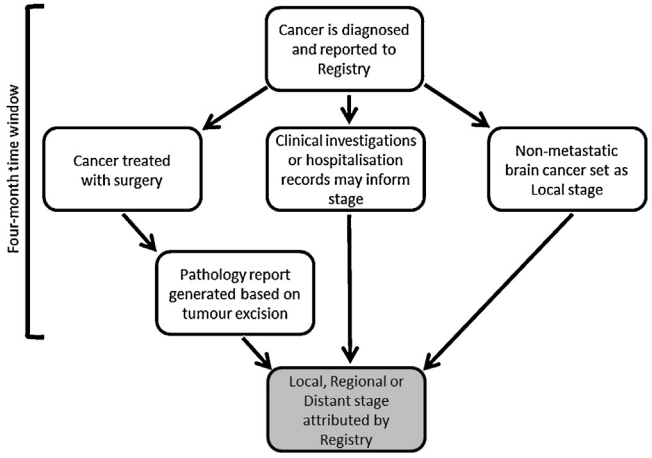

Fig. 1. Typical protocol for attributing cancer stage on the New Zealand Cancer Registry (NZCR).

the most commonly investigated [7,8,12–14,16]. Few studies have systematically investigated either the factors which predict a patient having unknown stage or the outcomes for these patients.

There are several reasons why stage of disease may be recorded as unknown:

(1) *Factors relating to cancer type*. Some cancers may be complex to stage, or the staging process may involve investigations – the results of which are not routinely collected by a cancer registry. Also, the staging process may extend beyond the post-diagnosis time window (typically 4 months) [17] required to be included as stage at diagnosis on a register. Thus, these patients may be adequately staged in reality, but their data are not formally included on a register.
(2) *Issues of data quality* where some services or clinical providers are more (or less) likely to provide data on staging to a central cancer registry.
(3) *Characteristics of the patient which are related to poor life expectancy*. In this case, clinicians may not stage the cancer because it is assumed that the patient is likely to die imminently or that a patient is unlikely to benefit from treatment. In this respect, both age and comorbidity have been consistently associated with a lower likelihood of being staged in other studies [1,6–9,11–13,16,18].
(4) *Characteristics of the patient which are associated with poorer access to or through quality health services*, which may therefore be associated with a lower likelihood of staging. There is considerable evidence that ethnic minority groups may fall into this category [19–22]. African-American and Māori ethnicity have been shown to increase the likelihood that a given patient would have unknown stage in the US and New Zealand contexts, respectively [1,7,16,23].

These four sets of factors are not mutually exclusive, and their relative contribution is likely to vary according to cancer type and population context.

Regarding treatment of patients with unknown stage, it remains unclear whether the link between unknown stage and lack of definitive treatment might be explained by comorbidity and/or advancing age – whereby patients who are in a poor physical state are not staged nor given treatment because they have a poor prognosis. It is also possible that there is an independent pathway between unknown stage and definitive treatment – whereby some patients do not receive definitive treatment because of inadequate staging. Lastly, perhaps those who do not receive definitive treatment – predominantly surgery – are less likely to have stage data collected by cancer registers. Again, these possibilities are not mutually exclusive, and have not been investigated.

In terms of outcomes for patients with unknown stage, there is evidence that these patients have survival probabilities intermediate between regional (extended to adjacent tissue or lymph nodes) and advanced (metastasised) disease [2,8,16]. However, the factors which may explain this pattern remain unexplored.

We are addressing four study questions in this paper:

1. What is the prevalence of patients with unknown stage amongst the most highly prevalent cancer sites within a population-based registry in New Zealand?
2. What factors are associated with having unknown stage on a cancer registry? Specifically, what is the role of sex, age, ethnicity and comorbidity?
3. What proportion of those with unknown stage receives surgical treatment compared to those with staged disease?
4. What is the survival experience of patients with unknown stage compared to those with staged disease both in terms of short term (28-day) and longer term (1-year) survival?

2. Patients and methods

2.1. Data sources

The New Zealand Cancer Registry (NZCR) is a collection of all new primary malignancies (except non-melanoma skin cancers) diagnosed nationwide, and was used to define the study cohorts. All patients diagnosed between 01/01/2006 and 01/09/2008 were initially included (n = 64,237). Patients were excluded if they had in situ or secondary tumours of unknown primary; lymphoma, myeloma or leukaemia; were non-New Zealand residents; had cancers diagnosed on or following date of death; or had cancers for which less than 400 patients were diagnosed over the study period.

Following exclusions, 18 cancer sites remained for further analysis (n = 41,489 patients). The basis on which diagnoses were recorded on the NZCR is available as supplementary material. Based on the proportion of patients with unknown stage, three non-intersecting groups of cancers emerged (Fig. 2): cancers with a 'low' (2–14% unknown stage, including kidney, thyroid, uterine, breast, colon, ovarian, skin melanoma, testis and brain cancers), 'moderate' (33–42%: cervix, lung, stomach, pancreas and rectal cancers); or 'high' proportion of patients with unknown stage (65–73%: prostate, bladder, liver and esophageal cancers). Subsequent analyses are presented both by individual cancer and also by the three groups identified above.

In order to determine comorbidity, receipt of definitive surgical treatment and mortality, NZCR data were linked with other routine health care datasets maintained by the New Zealand Ministry of Health. Data on comorbidity and receipt of definitive surgery were derived from the National Minimum Dataset (NMDS), which

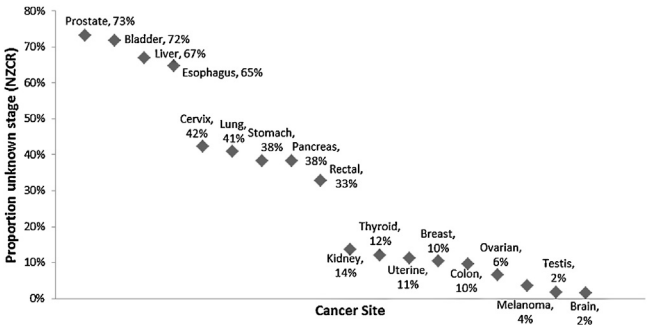

Fig. 2. Proportion of patients with unknown stage, by cancer site.