



EDITORIAL COMMENT

Register-based research. Accurate data and analysis, crucial for correct conclusions. Comment on “Incidence, mortality, and relative survival of patients with cancer of the bladder and upper urothelial tract in the Nordic countries between 1990 and 2019”

By retrieving data on incidence cases and deaths due to urothelial cancer in the bladder and the upper urinary tract (ureters and renal pelvis) in the Nordic countries between 1990 and 2019, Karttunen et al. have studied the changes in the incidence, mortality and relative survival over the mentioned time period, in a paper in the current issue of *Scand J. Urol.* [1]. The purpose was, according to the authors, to understand potential impact of new treatment options. The statistical analysis of the material revealed that the incidence was stable while mortality rates declined, and relative survival increased. Their conclusion was that those improvements may be due to earlier diagnosis and better treatments.

However, the speculations the authors have made on improved survival and mortality cannot be drawn from the data presented in the present study. To evaluate the impact of different treatment options one needs to understand the disease, know the value of different prognostic markers and study which tumour will respond to a certain treatment. In the present study urothelial bladder cancer (UBC), upper tract urothelial carcinoma (UTUC), high-risk and low-risk tumours, and different treatments, are all mixed as a salad in the same bowl.

UBC is a common disease. On the other hand, UTUC is relatively rare and represents 5–10% of all urothelial cancers [2]. Also, when studying urothelial carcinoma it is important to understand that although UBC and UTUC both derive from urothelial cells, they are different diseases [3]. UBC has been studied far more than UTUC and while some prognostic markers are relevant for both tumour types, the scientific findings known from research on UBC cannot be extrapolated to UTUC. During the last decade the impact of molecular markers have been elucidated. Several studies have shown that UBC and UTUC have different mutational patterns, underlining the importance of treating the diseases differently [4–6].

Tumour stage and grade have proven to be strong prognostic factors for both UBC and UTUC [2,7,8]. Concerning tumour stage, about 60% of UTUCs are invasive at diagnosis, as compared to 20–25% of UBCs. Tumour grade is also of utmost importance as it has been proven that how we grade the tumours, using WHO grading system 1973/1999 or 2004 or both, has prognostic value [9–11].

Since 2015 the European Guidelines for UTUC [2] divide UTUC into low- and high-risk UTUC based on certain criteria where tumour grade and stage are by far the strongest prognostic markers. The 5-year cancer specific survival (CSS) is less than 50% in the high-risk group and 80–90% in the low-

risk group. Provided organ-confined disease, the recommended treatment in the high-risk group is radical surgery with nephroureterectomy whereas organ sparing treatment is recommended to be considered in all low-risk cases [2]. These recommendations have changed dramatically over the study period in the present study. For UBC the treatment recommendations and CSS differ greatly between tumours that are low- or high-grade non-invasive or high-grade invasive [7,8]. Accordingly, a proper risk stratification is crucial not only for treatment decisions, but also for evaluating oncological outcome after different treatments.

In the Nordic countries we have a unique situation in that all countries have national social security numbers that can be used to track individuals and cross link various registers. We also have national and Nordic registers like the Nordic database of cancer statistics, NORDCAN, with high compliance of data reporting and disease registration. It is praiseworthy that the data on incidence and survival on patients with urothelial cancer in the Nordic countries have been studied by this group using NORDCAN.

However, the data from registers should be used carefully. One needs to keep in mind that the data that comes out of a database can only be as good as the data registered. From the data included in this study it is not possible to draw any conclusions on why the survival of patients with urothelial cancer has improved. Crucial prognostic markers, relevant for both UBC and UTUC, such as tumour grades and stages are missing in the analysis. There is no data on how different tumours were treated or followed up after treatment. Other known risk factors such as tobacco consumption and body mass index (BMI) are discussed but there is no data presented on these parameters.

The authors discuss the limitation pooling non-invasive and invasive tumours, and that non-invasive tumours are considered benign in Denmark and malignant in the other Nordic countries. Nevertheless, they conclude that the statistical analysis allows robust identification of long-term trends for urothelial carcinomas in the Nordic countries. The authors also mention that the data is collected from the pre-immunotherapy era and that improvements in survival may be due to better treatments. However, if the intention is to evaluate improvement due to earlier detection or different treatments, the data relevant to evaluate these variables as well as patient's characteristics need to be included in the analysis.

This is a message not only to investigators but also to those responsible for our national and Nordic databases. At

least in Sweden, the registration system for urothelial cancer is custom made for UBC but does not meet the needs for proper registration of UTUC. We should protect the fantastic possibilities with Nordic common databases for cancer statistics, i.e. protect the quality of these databases as well as how the data is used. One must keep in mind that while the results may be statistically coherent, they are not necessarily as relevant from a clinical point of view or valid from a scientific perspective.

Disclosure statement

No potential conflict of interest was reported by the author(s).

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