



EDITORIAL COMMENT

The devil is in the selected details: second-look resection in T1 bladder cancer

A Swedish population-based study on the effect of routine second-look resection in stage T1 bladder cancer was published earlier in 2021 [1]. The overall finding of this study is that survival outcomes in a cohort of patients with T1 bladder cancer not undergoing second-look resection were identical to those in a cohort of patients with T1 bladder cancer who routinely underwent second-look resection, as recommended in the guidelines. Despite their recognition of selection mechanisms in this population-based, non-randomized design, the authors conclude that a randomized study defining the role of second-look resection would be highly relevant.

In the present edition of *Scandinavian Journal of Urology*, another population-based study from another Nordic country has had the very same focus [2]. However, even though identical findings could be expected from neighboring countries, the authors of the Norwegian study conclude that the current recommended use of second-look resection in the European Association of Urology guidelines is supported. This conclusion is based on findings that second-look resection makes the histology more reliable, with impacts on treatment strategy and ultimately on survival. Therefore, one can potentially conclude that the Norwegian study does not support the need for a randomized study in the field and, conversely, that such a study implies a high risk of a poorer outcome for patients if they end up in the 'no second-look resection' arm.

How can two population-based studies from almost the same recent period have such diverging conclusions? With regard to population-based studies, it is imperative not only to look at the data included but also to recognize which essential data are missing.

The two cohorts seems to be comparable at first, with almost complete coverage in a 5-6 year period, leading to twice as many patients in the Swedish compared to the Norwegian study, as expected from differences in population size. However, almost the same number of patients undergo second-look resection in the two cohorts, i.e. 642 of 2456 in the Swedish cohort and 648 of 1130 in the Norwegian cohort. Therefore, the percentage of 'routine' second-look resection is as low as 26% in Sweden compared to 57% in Norway. In both cohorts, younger patients with minimal comorbidity are more frequent in the resected group compared to patients not undergoing second-look resection. This makes survival estimates somewhat uncertain *per se*, and other unadjusted tumor-specific factors are also likely to influence which patients undergo the second procedure.

Ultimately, the best way to justify a second-look resection policy from data in non-randomized population-based studies such as these will be to evaluate the histopathological findings at the second-look resection. The Norwegian authors have done this and elegantly show that there is a risk of understaging muscle-invasive disease if only one resection is

performed. This finding was most evident in patients without muscle in the first resection specimen. Moreover, they found that high tumor stage at restaging resection was negatively correlated with poor outcome as an individual risk factor. Based on this, restaging second-look resection seems imperative, as recommended in the current guidelines.

As opposed to this, there is no information on findings at second-look resection in the Swedish data. In contrast, the authors have excluded all patients who were upstaged to muscle-invasive disease at the restaging procedure. By doing so, the material naturally cannot show any benefit of second-look resection as the patients benefiting most from the procedure have been excluded from the cohort before they even enter it. The authors argue that by doing so, the non-resected cohort could have a false lower survival rate, as understaged muscle-invasive disease is still included in this group, whereas they are excluded from the resected group. Even though this, as a very theoretical concept, could be true, it is no argument for risking the life of patients with understaged muscle-invasive disease by allocating them to the placebo arm of a randomized clinical trial. Instead, our Swedish colleagues are urged to start registering the histopathological findings of second-look resection in their otherwise very comprehensive and useful database. This could then be used to evaluate whether we can avoid repeated procedures in the majority of T1 patients in the upcoming era of T1 substaging and *en bloc* resections. These two promising methods could make urologists better at selecting only the correct, low number of patients for a second-look resection in the future.

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Received 18 June 2021; accepted 21 June 2021

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