SCANDINAVIAN JOURNAL OF UROLOGY
2021, VOL. 55, NO. 1, 53
https://doi.org/10.1080/21681805.2020.1866661

EDITORIAL COMMENT

No 'one size fits all' approach in the management of high-risk non-muscle invasive bladder cancer

In this month's issue of SJUN Wang and colleagues analyzed cancer-specific survival (CSS) in patients with high-risk non-muscle invasive bladder cancer (HR NMIBC) following treatment with either BCG or radical cystectomy (RC) using data from the Swedish National Register of Urinary Bladder Cancer (SNRUBC) [1]. They found that patients treated with RC had worse CSS than patients treated with BCG.

This is a thought provoking article and challenges conventional thinking in this area: At first glance it is surprising by how much the data *appear* to show a benefit in favour of BCG. However the authors themselves freely acknowledge the limitations of such a study which are worth discussing first.

Clinical experience suggests that patients being offered (and accepting) primary RC tend to have particularly aggressive disease (multifocal disease, large volume disease, co-existing carcinoma *in situ* and variant histology). As the authors themselves acknowledge it is unfortunate that this data was not available to be included in the propensity scores and subsequent matching as this may likely be one explanation for the worse outcomes with RC. In addition no information is available on re-resection TURBT or upstaging at RC. Previous published studies of RC for NMIBC suggest that 20% of patients are upstaged to MIBC on pathological review [2] and knowing this information in the RC group who, as discussed above, may have had more aggressive disease would help to contextualize the inferior CSS seen with RC.

On the other hand, as the authors discuss, the reported survival advantage of RC in this setting up to now is also based on retrospective data which would likely introduce similar biases. However the only prospective randomized trial of BCG versus RC (BRAVO) failed to recruit [3].

Nevertheless some findings deserve comment. The majority of new patients diagnosed with HR NMIBC (56%) did not receive any further treatment. The database covers 1997–2014 and certainly in the late '90s BCG therapy was not universally administered. Although the authors also mention that the well known toxicity of BCG in the elderly may be part of the explanation I think that it wouldn't entirely explain this suboptimal treatment. Although it was not the aim of this study, it would also be interesting to know the CSS outcomes in this untreated group of patients to illustrate the natural history of HR NMIBC and put the reported outcomes of this study in context. Of patients who did receive treatment, 85% had BCG suggesting that some form of selection by urologists was already occurring. Finally, over the 17 years of the study the management of HR NMIBC has changed considerably (including the introduction of re-resection) and this in itself may make interpretation of the results difficult.

So what can we conclude from this study? Firstly, based on these data, urologists in Sweden appear to be very good at *selecting* which patients with HR NMIBC have a relatively good prognosis (and are therefore suitable for BCG) from those with a poorer prognosis (a proportion of whom will not be 'saved' by RC alone). Secondly, given these results and the known 20% understaging rate, RC alone appears inadequate for patients with HR NMIBC with the very worst prognosis. Perhaps these patients should be considered for neoadjuvant chemotherapy as they would be in if their disease was muscle-invasive from the outset. Nevertheless the authors are to be congratulated for challenging the dogma that patients with HR NMIBC *invariably* have better outcomes with cystectomy than BCG.

Disclosure statement

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

References

[1] Wang E, Larrson U, Gardmark T, et.al. Radical cystectomy compared to intravesical BCG immunotherapy for high-risk non-muscle invasive bladder cancer – is there a long-term survival difference? – Submitted to the SJUN (SJUN-2020-0606).

[2] Babjuk M, Burger M, Compérat EM, et al. European Association of Urology guidelines on non-muscle-invasive bladder cancer (TaT1 and carcinoma in situ) - 2019 update. Eur Urol. 2019;76(5): 639–657.

[3] Oughton JB, Poad H, Twiddy M, et al. Radical cystectomy (bladder removal) against intravesical BCG immunotherapy for high-risk non-muscle invasive bladder cancer (BRAVO): a protocol for a randomised controlled feasibility study. BMJ Open. 2017;7(8): e017913.

Hugh Mostafid*
Royal Surrey County Hospital, Guildford, UK
hugh.mostafid@nhs.net

Received 14 December 2020; Accepted 16 December 2020