Precision prostatectomy: reconciling functional and oncological outcomes

David Neal

Surgical oncologists need constantly to balance delivering the best long-term cancer-free outcomes against preserving function and facilitating rapid recovery. Minimally invasive surgical techniques and alternative methods of tissue ablation such as high-intensity focused ultrasound (HIFU), radio-frequency ablation, cryotherapy and laser-based photodynamic therapies are being tested to address this need. One major question is which men require radical treatment because without it they are at risk of progression, metastasis and death, and which men might be managed by careful monitoring. Another question addressed by this paper is whether some men with low or intermediate risk prostate cancer (PC) might wish to have surgical treatments which have an increased risk of leaving tumour behind, but which have better side effect profiles. The crucial question they raise, however, is whether the trade-off between better quality of life and the risks of leaving some residual local tumour can be safely calibrated. The reason this is important is because evidence from meta-analyses shows that positive margins are associated with increased rates of biochemical recurrence (by 35%–50%),1 in men having standard radical prostatectomy, although in T2 Gleason 6 disease, the increased risk of biochemical recurrence may be modest.

When new techniques are developed, researchers have an obligation to determine that they are safe and effective and that the process of introduction does not harm patients. These challenges are acute in the management of PCs. Sood and colleagues from the Vattikuti Urology Institute at the Henry Ford Hospital in Detroit describe in this issue of the journal a modification of existing techniques of robotic-assisted laparoscopic prostatectomy (RALP) for the treatment of localised PC. Do they pass the test?

Current evidence suggests that mp-MRI and targeted biopsy coupled with systematic biopsy is the most accurate way of identifying men with significant cancers at diagnosis.2–4 But how accurate are such approaches in picking up additional clinically significant cancers (Gleason Group ≥ 2) within a prostate known already to harbour a cancer? While the precise figure is open to debate, it is clear that men with clinically significant disease frequently harbour multifocal cancers. It is also clear that many of these cancers are missed by current diagnostic approaches and are distant from the ‘index’ cancer.5 6 Furthermore, it is now clear that within the prostate there are significant ‘field effects’ and that while some cancers have evolved from a single clone, others are truly polyclonal in origin.7 For these reasons, reservations continue to exist around the use of focal therapy where only the cancer(s) which can be seen (the index or dominant lesion) are treated. Conversely, the rationale for testing conservative approaches is that Active Surveillance is proven to be a valid approach for Gleason Grade Groups 1 and 2, since most low risk and intermediate risk PCs do not cause symptoms, metastasis and death within a 10-year time frame8 and many low and intermediate risk cancers stay of the same grade over time.9 However, it also clear that dedifferentiation can occur over time in some men.10 11

Progression and death rates in such men at 10 years are extremely low following surgery, radiotherapy and active surveillance9 and biochemical recurrence following surgery in Gleason Groups 1 and 2 is ~20% at 10 years,12 13 so measurement of safety for new approaches can only be defined in the long-term. Nevertheless, increased rates of early cancer recurrence are concerning. Another open biological question is if creating a wound within the prostate either by HIFU or partial prostatectomy, resulting in an environment rich in cytokines and growth factors, might actually promote long-term cancer growth if malignant cells are left behind.14

Menon and colleagues have tested the idea of carrying out a standard robotic-assisted
nerve-sparing radical prostatectomy on the side of the
main lesion and carrying out a fascial-preserving approach
on the contralateral side in a selected group of men who
might have been suitable for HIFU/focal therapy. The
purpose was to remove all the prostate and all the cancer
on the side of the dominant lesion; on the other side, the
fascia and a ‘thin rim of prostate’ (noted as 5mm in one
part of the manuscript and 5–10mm in another) were
deliberately left behind. They termed this partial removal
as ‘precision prostatectomy’.

A preliminary study of 100 radical prostatectomy
samples was carried out, modelling the presence of
cancer in the rim that would have been likely to be
preserved with ‘precision prostatectomy’ and therefore
what cancer would have been left behind after the new
operation. This exercise suggested that 35% would have
had cancer left behind, 14% having clinically significant
disease. However, only 25 of these 100 cases would have
been suitable for HIFU or focal therapy, which was one
inclusion criterion for the ensuing pilot clinical study of
eight men with good sexual function (four with Gleason 3+3; four with 3+4 disease). It is not clear from the paper
how many of these 25 men would have had cancer left
behind if they had undergone a ‘precision prostatecto-
y’. It was surprising to me that routine postoperative
mpMRI and modern imaging with PSMA PET-CT was
not performed or reported.

At 12 months, the functional results were excellent
with all men having good sexual function and contin-
ence. This compares with the authors’ previous potency
rates of ~80% following standard RALP (although ~50%
of the 80% used PGE-5 inhibitors). As far as cancer
outcomes are concerned, on the side of the ‘precis-
ion prostatectomy’ positive margins were found in
tree men (37.5%) including two of the four men with
Gleason 3+4=7 disease. These numbers are small, but in
these men with ≤T2 disease, they translate into pos-
tive margins in 50% of men with Gleason 3+4=7 disease
and 25% of men with Gleason 3+3=6 disease, which
may well seem concerning to many prostate surgeons.
At a very early follow-up at 12 months, two men (25%)
had biochemical recurrence and had residual prostate
volumes of 6mL with positive biopsies. Both of the
men with Gleason 3+4=7 disease and positive margins
had biochemical recurrence at 12 months. The authors
describe this as satisfactory, but these outcomes would
not generally be considered acceptable in a comparable
contemporary surgical series, particularly given the
short follow-up.

We should applaud efforts to improve the functional
outcomes of cancer surgery while preserving cancer recur-
rence rates, but unless a way can be found to accurately
identify those men who truly do not have cancer near the
fascia on the opposite side to the dominant lesion, such
approaches may carry increased risks of local recurrence.
Perhaps such procedures should be confined to only very
low risk men, although the majority of such men do well
without surgery.

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