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Reclassification due to upgrading during active surveillance protocols in low risk prostate cancer: The role of repeat biopsies in the long term

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Objectives

Repeat biopsies have a key role in Active Surveillance (AS) protocols aiming at the early detection of reclassification or progression during monitoring. We evaluate the proportion of upgrading in repeat biopsies during time, in an AS cohort of low risk prostate cancer (PCa) patients.

Patients and Methods

Since 2005, patients with low risk PCa who chose AS, were enrolled in the mono-institutional **SAINT** protocol. In November 2007 the international multi-center **PRIAS** (Prostate Cancer Research International Active Surveillance) protocol was also adopted (1, 2).

Eligibility criteria:

- clical stage ≤T2a
- initial PSA (iPSA) ≤10 ng/mL
- Gleason Pattern Score GPS ≤3+3, ≤25%
- positive cores with a maximum core length containing cancer ≤50% (SAINT) or ≤2 positive cores. 3+ positive cores if mpMRI and fusion biopsy confirms GS ≤3+3
- PSA density<0.2 ng/mL/cm3 (PRIAS)

Since 2016, multi-parametric MRI (mpMRI) with target biopsies has eliminated the criterion of the maximum number of positive biopsies.

Monitoring examinations and schedule:

- PSA every 3 months
- DRE every 6 months
- Biopsy at:
  - year 1, 4, 7 in PRIAS protocol
  - year 1, 2 then every 2 years in SAINT protocol.

Extrabiopsy was recommended when PSADT ranged between 3 and 10 yrs.

Triggers for treatment:

- GPS> 3+3 (Grade Group > 1)
- Positive cores: > 25% total cores in SAINT, >2 in PRIAS until 2016 (mpMRI/target biopsy implementation).
- PSADT < 3 yrs caused the exit from protocol until march 2015, advised extrabiopsy in the following years.

Results

From March 2005 to October 2018, 1036 patients were included in AS, 338 in SAINT and 698 in PRIAS protocols.

Overall, 1688 re-biopsies have been performed and 258 (15.3%) found out GPS > 3+3 tumors (upgrading). The proportion of reclassification remained stable during the study period, ranging from 11.9% to 19.7% (Figure). No significant differences were detected between timepoints (P= 0.62)

In the time window between 7th and 8th year, when a biopsy was planned in both protocols, 80 patients underwent biopsy, and 10 (12.5%) were upgraded.

In the previous years of AS, 46 out of 80 (57.5%) pts underwent just protocol scheduled biopsies, while 34 (42.5%) pts underwent additional PSADT-driven extrabiopsies (XBx). Upgrading occurred in 8/46 (17.4%) with no XBx and in 2/34 (5.9%) of those who had XBx (chi-squared 2.338, DF 1, p= 0.126).

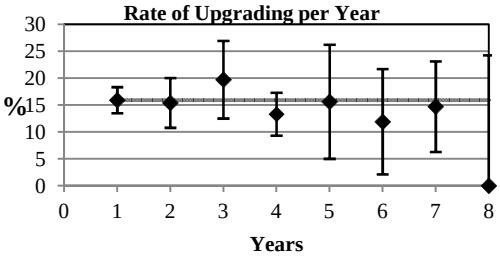

Figure: Rate of upgrading per year (C.I. 95% for proportion)

Conclusions

Proportion of upgrading ranges between 12% and 20% up to 8th year.

Surveillance pressure and multiple repeat biopsies seemes not to reduce the chance of harbouring high-grade disease during study period.

The biological meaning and clinical consequences of these findings remain uncertain, as no evidence is available in interpreting any differences between 'early' vs 'late' reclassified diseases.