Hypofractionated vs. conventionally fractionated radiotherapy for prostate cancer: A meta-analysis

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Objectives:

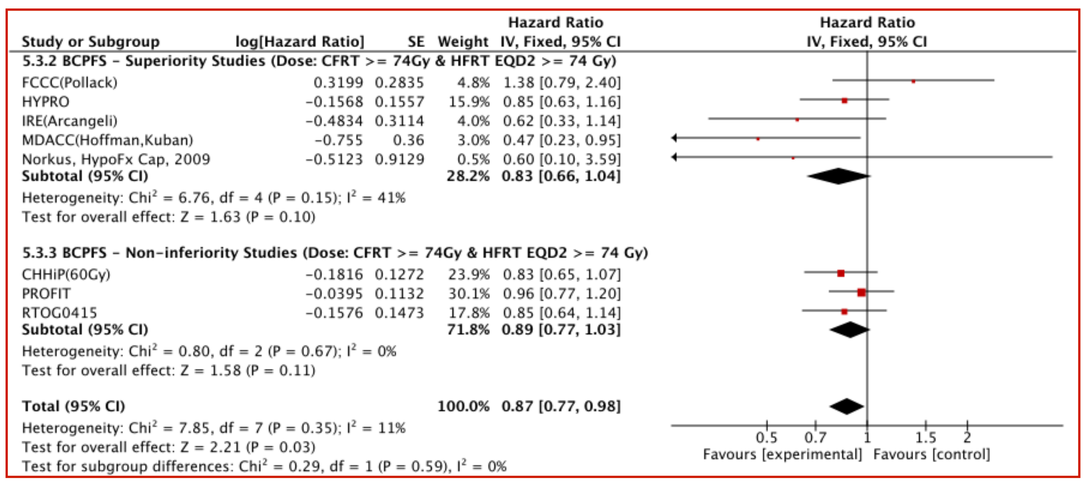
We conducted a meta-analysis of currently reported randomized clinical trials (RCT) to investigate the biochemical and/or clinical progression free survival (BCPFS) benefit and safety of hypofractionated radiotherapy (HFRT) compared to conventionally fractionated dose-escalated radiotherapy (CFRT) for localized prostate cancer.

Methods:

A comprehensive Medline and conference abstracts search was conducted to identify RCT reporting efficacy and toxicity of HFRT. Studies were included if they compared HFRT (2.4-4.5 Gy per fraction) with CFRT (1.8-2.0 Gy per fraction) for patients with localized prostate cancer. Studies that used CFRT dose less than 74 Gy or HFRT dose with EQD2 of less than 74 Gy, rounded to nearest whole number, were excluded. Primary endpoint was BCPFS defined as freedom from biochemical failure or clinical progression. Secondary endpoints were prostate-cancer specific survival, overall survival, and acute/late genitourinary (GU) and gastrointestinal (GI) toxicity. Hazard ratio (HR) was the effect size of choice for survival endpoints and odds ratio (OR) for toxicities. Event rates were assumed to be constant for HR estimations under the proportional hazard model. Either random-effects model (RE) or fixed-effect model (FE) was used based on the test of heterogeneity.

EFFICACY:

BCPFS:



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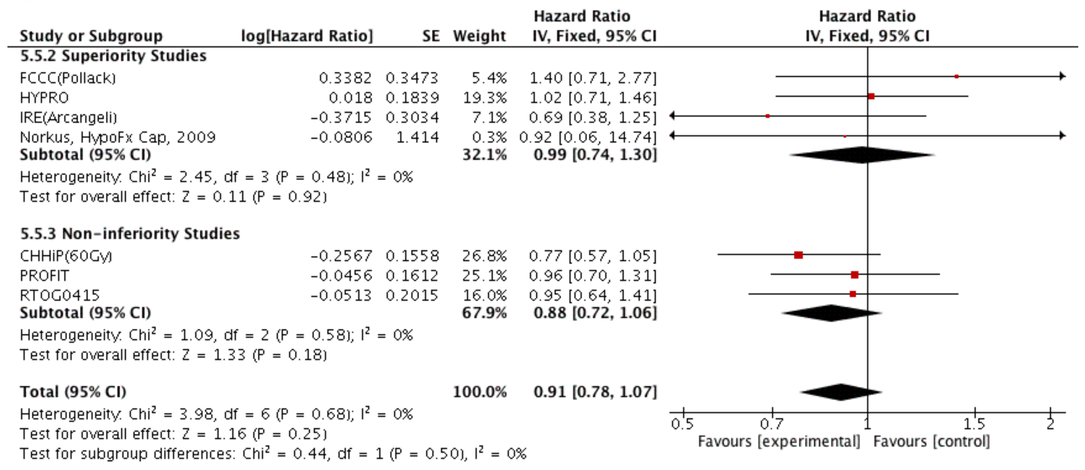

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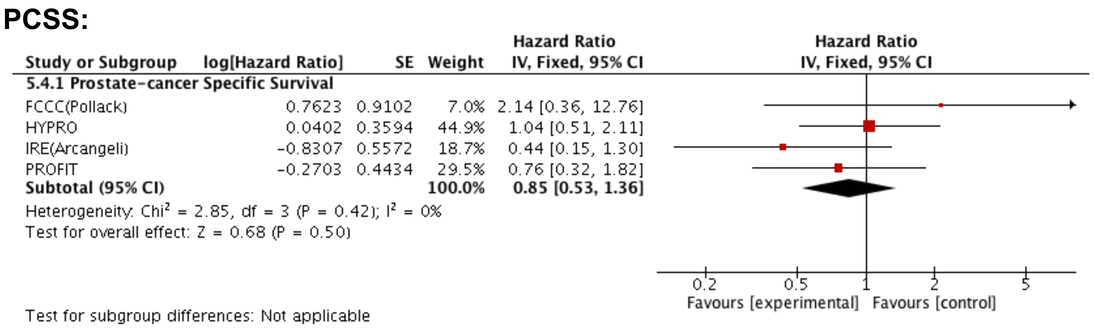
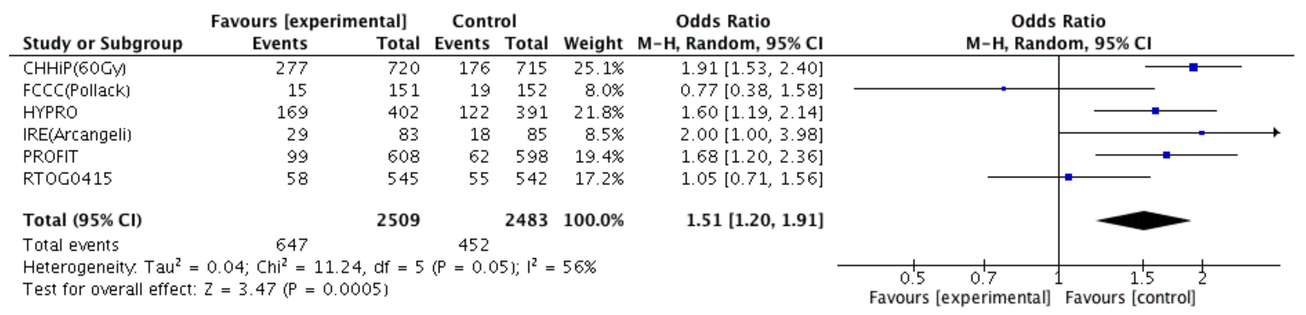


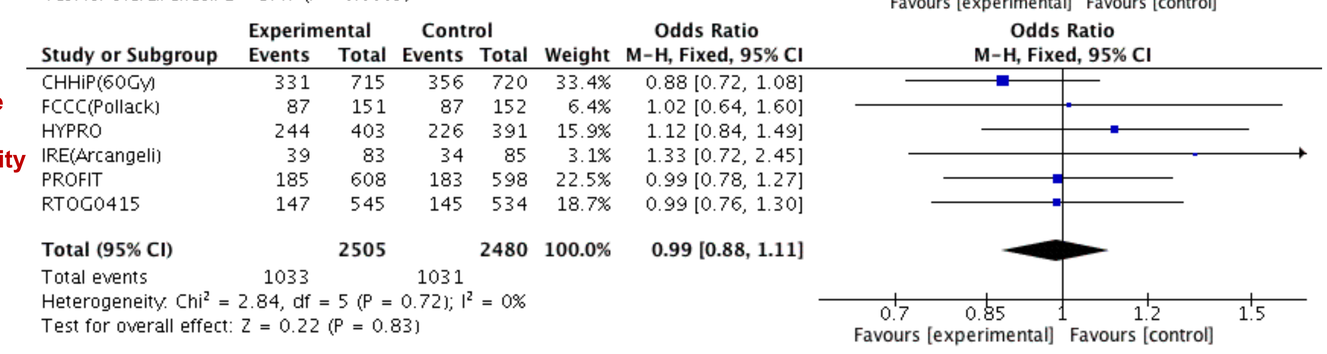
Test for subgroup differences: Not applicable

TOXICITY:

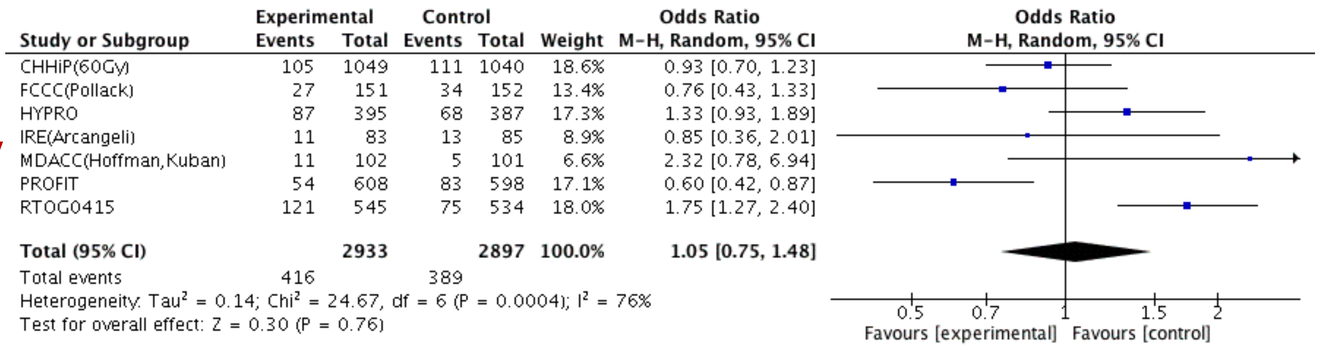
Acute GI Toxicity



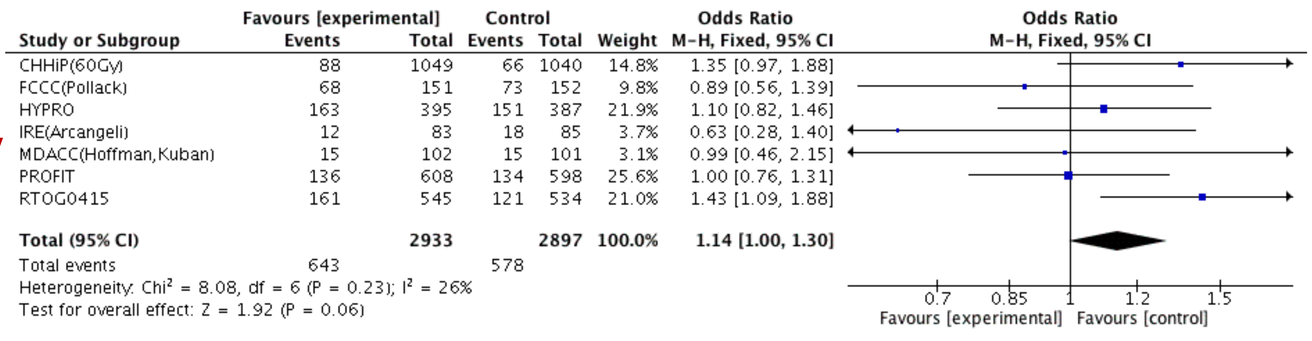
Acute GU Toxicity



Late GI Toxicity



Late GU Toxicity



Results:

- Eight RCT (CHHiP[1], Pollack[2], HYPRO[3], Arcangeli[4], Norkus[5], Hoffman[6], PROFIT[7] & RTOG0415[8]) were identified with total of 6007 patients.
- One of the two HFRT arms (i.e. 57 Gy in 19 fraction) in the three-arm CHHiP trial was excluded, as the EQD2 was less than 74 Gy.

EFFICACY:

- **Pooled analysis showed that the BCPFS was significantly better in the HFRT compared to CFRT (HR = 0.87; 95% CI: 0.77, 0.98, p=0.03, FE).**
- There was no difference in prostate-cancer specific survival (p=0.5, FE) or overall survival (p=0.25, FE).

TOXICITY:

- Patients treated with HFRT compared to CFRT, demonstrated:
  - statistically significant increased acute grade 2+ gastrointestinal toxicity (26% vs. 18%, OR=1.51, p=0.0005, RE)
  - no difference in grade 2+ acute genitourinary toxicity (41% vs. 42%, p=0.83, FE)
  - no difference in grade 2+ late gastrointestinal toxicity (14% vs. 13%, p=0.76,RE)
  - a trend toward worse grade 2+ late genitourinary toxicity (22% vs. 20%, OR=1.14, p=0.06, FE).

Conclusions:

- HFRT for localized prostate cancer results in statistically significant superior BCPFS when compared to CFRT.
- With currently reported follow up, there was no difference in prostate-cancer specific survival and overall survival.
- The improvements in biochemical control come at a modest and acceptable increase in acute and late toxicity
  - Grade 2+ acute GI toxicity was significantly higher with an absolute increase of 8% with HFRT and Grade 2+ late GU toxicities showed a trend toward worse outcome with HFRT.

References:

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