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FULL PAPER

Adjuvant and salvage radiation therapy after prostatectomy: investigating beliefs and practices of radiation oncologists

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Objective: Evidence regarding adjuvant radiation therapy (ART) and salvage radiation therapy (SRT) following radical prostatectomy (RP) for prostate cancer is inconsistent. The study objectives were to collect survey information on Italian radiation oncologists' (RO) beliefs regarding the use of ART and SRT following RP and to compare the results of Italian RO with those of American RO available from an analogous survey.

Methods: A modified version of a US-based questionnaire captured attitudes and clinical approaches regarding post-RP RT of all 716 RO practicing in 147 radiation oncology centres in Italy. Bivariate analyses compared the responses of Italian RO with those of American RO retrieved from a previously published study.

Results: Analysable questionnaires were completed by 153 Italian RO (response rate, 21%). Variations in practice were found for RT use, timing, dosage and technique. All

Italian RO supported ART use, although factors influencing the decision to initiate ART varied. Most RO (81%) would wait 3–6 months after surgery before beginning RT. Compared with Italian RO, more American RO believed ART improves survival outcomes (70% vs 35%, $p < 0.001$), would initiate ART based solely on adverse pathological features (79% vs 69%, $p < 0.001$) and would initiate SRT based on any detectable prostate-specific antigen (37% vs 11%, $p < 0.001$).

Conclusion: Italian RO strongly supported ART, but their approach to patient selection for ART and SRT varied. Striking differences between Italian RO and American RO regarding ART and SRT practices were found.

Advance in knowledge: Differential RT practices and perceptions exist among RO internationally. Clinical studies must inform evidence-based guidelines to harmonize the use of post-RP RT.

INTRODUCTION

Radical prostatectomy (RP) is a common evidence-based strategy for the treatment of localized prostate cancer. However, in patients with adverse pathological features (APF) such as seminal vesicle invasion (SVI), extracapsular extension (ECE) and positive surgical margin (PSM), RP is associated with a high recurrence rate ranging from 40% to 70%.¹ Adjuvant radiation therapy (ART) is administered soon after RP in the absence of sustained prostate-specific antigen (PSA) detection or a rise in PSA following an initial post-surgical reduction. Three randomized controlled trials have evaluated the effectiveness of ART, the Arbeitsgemeinschaft Radiologische Onkologie und Urologische Onkologie of the German Cancer Society (ARO/AUO) trial

in Germany,² the European Organization for Research and Treatment of Cancer (EORTC) trial³ and the Southwest Oncology Group (SWOG) trial in the USA.⁴ All three trials documented increases in biochemical relapse-free survival compared with observation alone among patients with one or more APF;^{2–4} only SWOG demonstrated improvement in metastases-free survival and overall survival.⁵ Genitourinary (GU) and gastrointestinal (GI) adverse effects were more common in patients receiving radiation therapy (RT), but few grade 3 or 4 toxicities occurred in either group.^{2–4}

Despite this evidence for ART, many clinicians instead rely on salvage radiation therapy (SRT), where RT is only initiated upon a rising PSA following RP. This may be due to

multiple factors including feared toxicity, risk of overtreatment, as well as an assumed equivalent clinical benefit of ART and SRT.⁶ Less than 20% of patients in the USA have been estimated to receive ART, and utilization did not increase significantly after the results of the prospective trials were published.^{7,8}

We conducted a national web-based survey of Italian radiation oncologists (RO) to assess the practice of RT following RP in Italy. Additionally, we sought to compare the survey results of Italian RO with those of American RO available from an analogous survey study⁹ in order to understand international similarities and differences in RT practices. We hypothesized that the lack of definitive evidence on how and when to use post-operative radiation therapy (PORT; ART or SRT) would result in significant variability in responses among RO within Italy, as well as significant international differences in practice.

METHODS AND MATERIALS

Participants and survey distribution

All 716 Italian RO practicing in the 147 radiation oncology centres that were listed in the Italian Association of Radiation Oncology (AIRO) roster (accessed January 2012) were sent an e-mail invitation from AIRO in February 2012. The survey invitation contained a brief introductory message and a link to the web-based instrument. To encourage participation, AIRO co-ordinated two follow-up e-mails to all participants within 1 month of the initial e-mailing. No honorarium was offered; participation was voluntary and anonymous. The link to the survey was closed 6 weeks after the initial e-mail invitation.

Survey instrument

The investigators designed the survey instrument using a US-based questionnaire as a framework. The questionnaire was previously used in an analogous published survey study and was provided for use in this study.⁹ The final survey consisted of a total 33 questions requiring approximately 10 min to complete. Besides demographics, survey domains included the following: beliefs regarding effectiveness of ART, selection criteria for ART, timing of ART, PSA threshold for SRT, estimated impact of RT on toxicity rates, details of surgical technique, RT technique and dosing and use of hormone therapy (HT) (Supplemental Material A). The survey was provided in English using an online survey service (surveymonkey.com) and also on the AIRO website.

Statistical analyses

Italian RO who had treated five or more patients with prostate cancer in the previous year and who also responded to questions regarding perceived effectiveness of ART were included for analysis. Descriptive statistics were generated for all variables of interest. To compare responses on beliefs surrounding the use of ART and SRT as well as perceived toxicity of RT between Italian RO and American RO, the research team utilized the original American survey data. Differences between Italian RO and American RO responses were evaluated using the χ^2 and Fisher exact test as appropriate. Data were analysed using SAS statistical software v. 9.2 (SAS Institute Inc., Cary, NC). The study protocol was reviewed and deemed exempt by Thomas Jefferson University's Institutional Review Board.

RESULTS

A total of 158 participants responded (overall response rate, 22%). Of them, four were excluded because of incomplete data on ART attitudes and one was excluded because he/she reported to have treated less than five patients with prostate cancer in the previous year. This resulted in an analysable sample of 153 questionnaires (response rate, 21%). Practice and clinician demographic characteristics are presented in [Table 1](#).

Adjuvant radiation therapy beliefs and practices

All Italian RO reported routinely recommending ART following RP, but under different circumstances ([Table 2](#)). 69% of respondents recommended ART based on APF in the RP specimen alone, whereas 29% reported using ART only in the presence of both APF and other features such as high Gleason score (GS) and post-operative PSA value. About one-third (35%) of respondents believed that ART improves overall survival rates, but the majority (65%) believed that ART does not provide a survival benefit. When RO were asked which factor by itself would form the basis for recommendation of ART (multiple selections were permitted), 92% of them reported PSM, 66% reported SVI, 66% reported ECE, 7% reported GS 8–10 and 2% reported detectable PSA after surgery. When asked about the timing of ART, the majority of RO (81%) recommended initiating ART 3–6 months following surgery in order to allow time for post-operative urinary recovery ([Table 2](#)).

Salvage radiation therapy practices

The beliefs of RO regarding initiation of SRT following a rise in PSA varied significantly ([Table 2](#)), with the most common threshold for beginning SRT reported as either a PSA of 0.2–0.3 ng ml⁻¹ (43%) or 0.4–0.5 ng ml⁻¹ (23%).

Radiation details

The most commonly reported radiation planning technique was three-dimensional conformal RT (3DCRT) involving >4 fields (58%), followed by intensity-modulated RT (IMRT; 46%) ([Table 3](#)). Larger radiation doses were reported more frequently for SRT (72% \geq 70 Gy) and ART with surgical margin involvement (72% \geq 70 Gy) than for ART for ECE or SVI (41% \geq 70 Gy). Weekly portal films were reported as the most frequently utilized image guidance strategy (60%) ([Table 4](#)). The clinical target volume to planning target volume margin lacked consensus; 34% of RO reported using a variable margin. Of RO who indicated use of a variable margin, 53% selected a posterior margin of 4–5 mm.

Perceptions of toxicity

The perception of PORT-related toxicity was inconsistent across functional areas, as 20%, 35% and 49% of RO conveyed beliefs of a moderate to major negative effect on urinary continence recovery, sexual function recovery and bladder neck contracture incidence, respectively ([Table 2](#)). When asked the extent to which patients receiving ART experience late toxicity, 51% of RO reported \leq 10% of patients, 26% reported between 11% and 20% of patients and 23% reported >20% of patients. If late toxicity occurs, RO designated the rectum, bladder and urethra as primary sites (64%, 23% and 13%, respectively).

Hormone therapy

If ART is initiated, the majority (54%) of RO reported advising their patients to start HT concurrently if residual disease

Table 1. Demographic characteristics of Italian and American radiation oncologists (RO)

Characteristic	Italian RO (N = 153), ^a n (%)	American RO (N = 218), ^{a,b} n (%)	p-value ^c
RO characteristics			
Gender			
Male	80 (52)	–	
Female	73 (48)	–	
Years in practice ^d			
≤10	70 (46)	90 (41)	0.50
11–20	41 (27)	71 (33)	
≥21	40 (26)	57 (26)	
Number of patients with prostate cancer treated in previous year			
5–10	5 (3)	–	
11–20	17 (11)	–	
>20	131 (86)	–	
Participation in co-operative group trials ^d			
Yes	18 (12)	116 (53)	<0.01
No	134 (88)	102 (47)	
Frequency of meeting with pathologist to review prostatectomy specimen			
Always (>90% of cases)	9 (6)	–	
Most of the time (60–90% of cases)	6 (4)	–	
About half of the time (40–59% of cases)	7 (5)	–	
Occasionally (10–39% of cases)	55 (36)	–	
Rarely (<10% of cases)	76 (50)	–	
Practice characteristics			
Academic practice setting			
Yes	28 (18)	69 (32)	<0.01
No	125 (82)	149 (68)	
Practice location (region of Italy) ^d			
North	78 (54)	–	
Central	34 (23)	–	
South	34 (23)	–	

^aPercent sum may not be 100% owing to rounding.

^bAmerican RO data are not presented for certain characteristics owing to survey differences.

^cp-values using the two-sided χ^2 test.

^dDenominators vary based on available responses.

(microscopic or macroscopic), stage disease (ECE or SVI) and a high GS (>7) are all present (Table 5). Most RO (70%) who recommend HT reported advising patients to continue HT for a period of 2 years. Responses of Italian RO regarding PSA and testosterone monitoring during HT differed substantially (Table 6).

Comparison of Italian and American radiation oncologists

A greater percentage of American RO practiced in academia compared with Italian RO (Table 1). Italian and American respondents were similarly distributed in terms of practice experience, but significantly, more American RO than Italian RO

reported participating in co-operative group trials (53% and 12%, respectively).

A significantly greater proportion of American respondents than Italian respondents believed that ART improves overall survival outcomes (70% vs 35%, $p < 0.001$) (Table 2). Differences between Italian RO and American RO existed in the parameters for recommending ART after RP. Most Italian and American RO recommended ART based on APF alone (69% vs 78%), but more Italian RO than American RO recommended ART only if both APF and other factors (high GS or post-operative PSA value) were present (29% vs 13%, $p < 0.001$). The majority of

Table 2. Responses by Italian and US radiation oncologists (RO) regarding recommendations for post-operative radiation therapy (PORT) and perceptions of radiation toxicity

Response	Italian RO (N = 153), ^a n (%)	American RO (N = 218), ^a n (%)	p-value ^b
ART			
Effect of ART on patient outcomes ^c			
ART improves overall survival rates	54 (35)	150 (70)	<0.01
ART improves biochemical control but not survival	99 (65)	63 (30)	
Factors to initiate ART ^c			
Based on APF alone	105 (69)	166 (78)	<0.01
Based on APF and GS/PSA	44 (29)	28 (13)	
If PSA is detectable	4 (3)	15 (7)	
Would never use ART	0 (0)	4 (2)	
Longest interval to ART initiation ^c (months)			
<3	23 (15)	8 (4)	<0.01
3–6	120 (78)	149 (70)	
>6	6 (4)	56 (26)	
SRT			
PSA threshold to initiate SRT ^c (ng ml ⁻¹)			
Any detectable	17 (11)	78 (37)	<0.01
0.2–0.3	65 (42)	106 (50)	
0.4–0.5	35 (23)	19 (9)	
0.6–0.8	14 (9)	7 (3)	
≥0.9	17 (11)	2 (1)	
Would never recommend SRT	3 (2)	0 (0)	
PORT			
Perceptions of toxicity ^c			
PORT has no/minor effect on urinary continence recovery for >50% of patients	90 (80)	116 (71)	0.11
PORT has major/total effect on urinary continence recovery for >50% of patients	23 (20)	47 (29)	
PORT has no/minor effect on sexual function recovery for >50% of patients	69 (65)	96 (59)	0.36
PORT has major/total effect on sexual function recovery for >50% of patients	38 (35)	67 (41)	
PORT has no/mild effect on incidence of BNC	70 (51)	126 (72)	<0.01
PORT has moderate/severe effect on incidence of BNC	66 (49)	48 (28)	

APF, adverse pathological features; ART, adjuvant radiation therapy; BNC, bladder neck contracture; GS, Gleason score; PSA, prostate-specific antigen; SRT, salvage radiation therapy.

^aPercent sum may not be 100% due to rounding.

^bp-values using the two-sided χ^2 test or Fisher exact test for cell value <5.

^cDenominators vary based on available responses.

Italian and American RO reported waiting between 3 and 6 months following RP to initiate ART (81% vs 70%), but a larger percentage of American RO were willing to wait more than 6 months than were Italian RO (26% vs 4%, $p < 0.001$).

The largest proportion of both Italian and American RO would initiate SRT in the range of 0.2–0.3 ng ml⁻¹ (43% vs 50%), but American RO were significantly more likely than Italian RO to initiate SRT at any detectable PSA (37% vs 11%, $p < 0.001$).

Table 3. Responses by Italian radiation oncologists (RO) regarding radiation technique and dosing

Response	Italian RO (N = 153), ^a n (%)
Radiation planning technique ^b	
3D conformal ≤4 fields	50 (33)
3D conformal >4 fields	88 (58)
IMRT	71 (46)
Arc therapy	27 (18)
Tomotherapy	9 (6)
ART	
Radiation dose (standard fractionation) for R0 ^{c,d} (Gy)	
<64	7 (5)
64–66.6	58 (38)
68–68.4	16 (11)
≥70	63 (41)
Hypofractionation	8 (5)
Radiation dose (standard fractionation) for R1 ^{d,e} (Gy)	
64–66.6	23 (15)
68–68.4	11 (7)
≥70	110 (72)
Hypofractionation	8 (5)
SRT	
Radiation dose (standard fractionation) ^d (Gy)	
<64	2 (1)
64–66.6	29 (19)
68–68.4	5 (3)
≥70	109 (72)
Hypofractionation	7 (5)

3D, three dimension; ART, adjuvant radiation therapy; IMRT, intensity-modulated RT; SRT, salvage radiation therapy.

^aPercent sum may not be 100% owing to rounding.

^bRespondents were allowed to select ≥1 radiation planning techniques; percentage sum exceeds 100%.

^cRadiation dose used for extracapsular extension or seminal vesicle invasion.

^dDenominators vary based on available responses.

^eRadiation dose used for positive surgical margin.

There was no statistically significant difference between Italian RO and American RO opinions on PORT's effect on urinary continence or erectile dysfunction recovery. However, a greater proportion of American RO than Italian RO believe that PORT has no or minor impact on the incidence of bladder neck contracture (72% vs 51%, $p < 0.001$).

In light of significant differences between countries in the proportion of respondents affiliated with academic institutions and reporting participation in co-operative group trials, we performed *post hoc* stratified analyses to evaluate whether practice patterns differed based upon these two characteristics. No significant

differences were found with regard to the survey items addressing survival outcomes with ART, the PSA threshold to initiate SRT or factors to initiate ART.

DISCUSSION

This work adds to the existing literature^{9–11} describing RO beliefs and practices regarding ART and SRT after prostatectomy. In accordance with RO preferences documented previously,^{9–11} Italian RO in the present study strongly supported the use of ART after RP, but their attitude towards timing, duration and dosage varied substantially. The absence of uniform guidelines^{12–14} delineating the appropriate PORT strategy for discrete and well-defined patient populations likely contributes to a practice environment characterized by individual interpretation of the literature.^{2–4} Differences in resources including equipment, reimbursement and staffing, as well as cultural and clinical considerations may also affect the treatment determination following RP. Our results reflect this confluence of factors that exist both within Italy and internationally.

Only 35% of Italian RO in our study indicated a belief of improved survival outcomes with ART, suggesting that the SWOG trial provided insufficient evidence to uniformly convince Italian RO of improved overall survival rates.^{4,5} Emphasizing potential differences in the interpretation and acceptance of international literature,^{2–4} 70% of American RO reported beliefs in improved survival outcomes with ART. The responses to this survey item may have been influenced more strongly by the evidence generated within each country or region. Multiple Italian institutions participated as trial sites in EORTC trial, which did not report a long-term survival benefit with ART.^{3,15} The SWOG trial, conducted in the USA, did report a survival benefit.⁵

Italian and American RO both generally recommend ART based upon APF alone (69% and 78%, respectively). Despite this principal finding, a greater proportion of Italian RO than American RO (29% vs 13%, $p < 0.001$) would recommend ART only in the presence of both APF and either an elevated GS or post-operative PSA value. Although preliminary data exist in support of PSA and GS as risk factors for disease relapse,^{2,5,16} insufficient evidence has been published to support the use of GS or PSA as a predictor of benefit from ART. Surgical margin status is the leading prognostic factor for predicting biochemical relapse-free survival and local relapse, independent of other risk factors.¹⁵ The prognostic significance of pathological details such as the extent or number of PSM remains uncertain and requires further investigation.¹⁷ In the absence of requisite data, the practice of requiring additional risk factors for ART recommendation is of concern. Our survey results also indicated that only 15% of Italian RO meet frequently with a pathologist to review prostatectomy specimens. Considering the prognostic significance of PSM, we believe that a multidisciplinary approach for defining surgical margin status is warranted.

The interval following RP prior to ART initiation was most frequently reported as 3–6 months by Italian (81%) and American RO (70%). Worryingly, more than a quarter (26%) of American RO reported waiting more than 6 months. The prospective clinical trials administered ART within 3–4 months of RP.^{2–4}

Table 4. Responses by Italian radiation oncologists (RO) regarding imaging methods and margin definition

Response	Italian RO (N = 153), ^a n (%)
Image guidance method for RP ^b	
Weekly port films	90 (60)
Daily port films without fiducial markers or clips	13 (9)
Daily port films with fiducial markers or clips	3 (2)
Cone beam CT	44 (29)
CT-on-rails	1 (1)
Ultrasound	–
Use of endorectal balloon ^b	
No	145 (97)
Sometimes	5 (3)
CTV to PTV margin ^b	
<3 mm	0 (0)
3 mm	4 (3)
4–5 mm	23 (15)
6–7 mm	20 (13)
8–9 mm	18 (12)
1.0 cm	31 (20)
1.1–1.5 cm	4 (3)
Variable	52 (34)
If variable CTV to PTV, what posterior margin? ^b	
<3 mm	2 (2)
3 mm	15 (11)
4–5 mm	70 (53)
6–7 mm	31 (23)
8–9 mm	14 (11)
1.0 cm	1 (1)

CTV, clinical target volume; PTV, planning target volume; RP, radical prostatectomy.

^aPercent sum may not be 100% due to rounding.

^bDenominators vary based on available responses.

There are no data supporting the use of ART after more than 6 months except when allowing for recovery from acute side effects of surgery.⁶ Otherwise, ART is not indicated at this extended interval, and monitoring for biochemical failure to initiate SRT is more clinically appropriate.^{10,12}

The dosing of PORT is expected to vary depending upon the indication for treatment, ART or SRT, but dose selection must also incorporate the functional status and toxicity tolerance of the patient.¹² The optimal ART dose for ensuring local control remains uncertain.¹⁸ The dose utilized in the three randomized trials ranged from 60 to 64 Gy, yet 25% of enrolled patients

developed a biochemical recurrence within 5 years at these dosages.^{2–4} This may represent a need for use of a dose-escalation approach; retrospective studies employing a total dose of at least 70 Gy have demonstrated a significant advantage in terms of disease-free survival.^{18,19} A minimum ART dose of 64–65 Gy has been recommended by the American Urological Association and American Society for Radiation Oncology Guideline Panel, who have also acknowledged the evidence for safety and improved tumour control with doses >65 Gy.¹² Recognizing the need for dosage individualization based on patient status, 72% of Italian RO reported using a dose of at least 70 Gy in the presence of PSM. An equal proportion of Italian RO (72%) reported using at least 70 Gy for SRT, in line with evidence supporting improved outcomes at higher doses.²⁰

Regarding the radiation planning technique, Italian RO reported to use 3DCRT with >4 fields (58%), followed by IMRT (46%) and 3DCRT with <4 fields (33%). Inconsistent availability of IMRT among RO practices and insufficient evidence of clinical superiority likely contribute to the more prevalent use of 3DCRT in Italy, which was also identified in a previous survey of Italian RO.¹¹ Although potential advantages including reduction of GI toxicities have been associated with IMRT,^{21,22} the published literature¹² does not reflect the implementation of newer radiation techniques in the adjuvant setting, and insufficient evidence exists to confirm a definitive advantage with IMRT over 3DCRT for toxicity and clinical outcomes.

Despite the fact that the survey responses between Italian RO and American RO are not technically comparable because of differential structure of the survey question (Italian survey item: single response; American survey item: multiple response), it is of note that 87% of American RO surveyed by Showalter et al⁹ reported use of IMRT relative to only 9% 3DCRT. American RO overwhelming use of IMRT is in stark contrast to the prevailing use of 3DCRT by RO in Italy. One explanatory hypothesis for this dissimilarity relates to reimbursement incentives present for American RO practices, which are considerably less influential on Italian RO practicing in a public healthcare system. Alternatively, potential benefits of IMRT including reduction of GI toxicities may be perceived differently between RO in each country.

A primary criticism of ART is the potential for unnecessary exposure of patients whose prostate cancer may never have recurred to RT-related toxicities, yet the tolerability of ART remains unclear. In the SWOG trial, both urethral stricture and urinary incontinence were more common among patients who received ART.⁴ By contrast, an interim analysis of the EORTC trial did not show an increased risk of urinary incontinence with ART.²³ No difference in the incident of urethral stricture was found in the ARO/AUO trial, which is the only study that used 3DCRT.² Moreover, data from observational studies using 3DCRT have not shown significant grade 3 late GI or GU toxicities.^{12,19} Perceptions of PORT toxicities were similar between American RO and Italian RO regarding urinary continence and sexual function recovery. A statistically and likely clinically significant difference in perceived effect of PORT on bladder neck contracture incidence was observed; 49% of Italian RO reported beliefs of a moderate/severe effect compared with

Table 5. Responses by Italian radiation oncologists (RO) regarding hormone therapy (HT)

Response	Italian RO (N = 153), ^a n (%)
Advise patients beginning ART Post RP to start HT ^b	
Yes, always	13 (9)
Yes, only when there is residual disease ^c	17 (12)
Yes, only when there is residual disease ^c and stage disease ^d	22 (15)
Yes, only when there is residual disease ^c , stage disease ^d and a high GS (>7)	80 (54)
Never	16 (11)
Suggested duration if HT is given ^b (years)	
≤1	31 (22)
2	98 (70)
3	4 (3)
Depends on risk factors	8 (6)
Percentage of patients discontinuing HT early owing to adverse effects	
≤10	129 (84)
11–20	16 (10)
>20	8 (5)

ART, adjuvant radiation therapy; GS, Gleason score; RP, radical prostatectomy.

^aPercent sum may not be 100% owing to rounding.

^bDenominators vary based on available responses.

^cResidual disease includes microscopic and macroscopic disease.

^dStage disease includes extracapsular invasion or vesicle invasion.

28% of American RO. Additional anticipated toxicity may influence the decision of Italian RO to reserve ART for patients with multiple risk factors for relapse.

Several factors likely influence the attitudes of RO towards ART and SRT, with both approaches possibly justified. Apart from patients with SVI, recurrences after RP are usually local.²⁴ Therefore, early local treatment may prevent locoregional diffusion. Additionally, since ART is administered for undetectable disease, it may be effective at lower doses than SRT.²⁵ The chief benefit of SRT is the avoidance of overtreatment of patients who are not destined to recur. Substantial variability exists with regards to the timing of SRT initiation, with the largest proportion of Italian RO having identified 0.2–0.3 ng ml⁻¹ as the PSA threshold for beginning SRT. Greater inconsistency was apparent internationally, as 37% of American RO would recommend SRT at any detectable PSA compared with only 11% of Italian RO. Improved outcomes following SRT have been attained when RT was initiated earlier, notably at any detectable PSA and in the presence of a slower PSA doubling time.^{16,24} Observational studies^{16,26} have suggested that SRT reduces PSA recurrence, distant metastases and prostate cancer-specific death, but the use of SRT is not presently supported by evidence from randomized controlled trials.

The role of concurrent ART and HT after RP is unclear. Our study found HT to be recommended under varying circumstances by

89% of surveyed RO, with most practitioners (54%) advising HT for patients at high risk due to residual disease (microscopic or macroscopic), ECE or SVI and a high GS (>7). Similar results of a 2011 survey of Canadian RO indicated that approximately half of the RO (55%) would recommend HT to high-risk patients.¹⁰ The 2-year duration of HT selected most frequently in our study (70%) was aligned with limited evidence supporting concurrent ART and HT.¹⁹ Interim results of a randomized controlled trial investigating concurrent SRT and 2 years of HT post RP demonstrated longer freedom from biochemical progression and a reduction in metastases; longer follow-up is required to determine the significance of an overall survival benefit.²⁷

In summary, the results of our survey of Italian RO taken contextually with previous surveys of American⁹ and Canadian¹⁰ RO underscore the large magnitude international variation in post-RP use of RT. Our results support the hypothesis that a large amount of variability in the use of PORT is derived from RO practice, which is based upon insufficient evidence in the published literature^{2–4} and a corresponding lack of definitive practice guidelines.^{12–14} Nonetheless, additional variation due to the structure of healthcare systems, as well as individual or societal preferences, likely exists. Academic and professional educational curricula, cultural values, reimbursement incentives and the availability of new technology each have the potential to contribute to distinct local and national practice environments. Furthermore, patient reported preferences are expected to impact treatment decisions. Future investigations are necessary to prospectively evaluate real-world use of ART and SRT for comparison with subjectively reported RO preferences while also characterizing the influence of societal and patient factors on PORT utilization.

This study has limitations. A primary limitation of survey methodology was the focus upon physician preferences, which were subject to reporting bias and may inaccurately represent actual RT utilization. Furthermore, our survey only captured the preferences and practice patterns of RO. Evaluating the practice patterns of urologists would be important to understand the management of the overall patient population with prostate cancer and the characteristics of patients referred by urologists for RO treatment. It is also important to acknowledge the period of time (approximately 1.5 years) separating the administration of the American and Italian surveys, during which time the dissemination of evidence may have contributed to differences in practice patterns observed between countries. Furthermore, time has passed since the survey was administered and practice patterns may have evolved.

A potential limitation stems from the absence of information regarding RO speciality within the AIRO list, since ideally we would survey only RO with a stated speciality in GU cancers. To overcome this limitation, we restricted our analytic sample to Italian RO who had treated at least five patients with prostate cancer in the previous year. Furthermore, the majority (86%) of RO (Table 1) reported treating >20 patients in that timeframe, indicative of extensive experience among sampled RO. The AIRO list contained 147 Italian radiation oncology centres, and we anticipate that one to two RO with experience treating

Table 6. Responses by Italian radiation oncologists (RO) regarding monitoring during hormone therapy (HT)

Response	Italian RO (N = 153), ^a n (%)
Frequency of PSA monitoring during HT ^b	
Every 2–3 months	66 (46)
Every 4–5 months	40 (28)
Every 6 months	39 (27)
Frequency of testosterone monitoring during HT ^b	
Every 2–3 months	14 (13)
Every 4–5 months	5 (5)
Every 6 months	54 (50)
Every 7–9 months	3 (3)
Every 10–12 months	15 (14)
Less than once per year	18 (17)
Target testosterone level during HT ^b (ng ml ⁻¹)	
≤20	66 (48)
≤50	13 (9)
≤100	3 (2)
≤150	2 (2)
No specific target	54 (39)

PSA, prostate-specific antigen.

^aPercent sum may not be 100% owing to rounding.

^bDenominators vary based on available responses.

prostate cancer were practicing at each centre. Considering the 153 responses we received in the context of 147 Italian radiation

oncology centres, we are confident that the responses of sampled RO are representative of the beliefs and ongoing practices of RO treating prostate cancer in Italy.

The survey of American RO was conducted separately prior to our research, but while it was not identical, the American survey tool was highly conserved and provided the framework for our survey. To prevent the introduction of bias, comparisons using data from the American RO study were only made on survey items that remained entirely consistent across both studies (Tables 1 and 2).

CONCLUSION

This national survey of Italian RO highlights the considerable agreement among Italian RO regarding ART's use after RP based upon APF while also emphasizing differential PORT practices and perceptions both within Italy and internationally. Further research should focus on informing the joint clinician–patient decision regarding RT after RP by defining high-risk patient populations for which ART is appropriate. Ongoing studies [(e.g. Radiotherapy-Adjuvant Versus Early Salvage (RAVES), Radiotherapy and Androgen Deprivation in Combination After Local Surgery (RADICALS)] comparing ART with SRT post RP are necessary to better define such populations and characterize the toxicity burden associated with newer treatment modalities (i.e. IMRT), ensuring that the quality of life is appropriately considered alongside clinical and survival outcomes in future treatment algorithms.

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