Randomized Controlled Trial of a Computerized Decision Aid on Adjuvant Radioactive Iodine Treatment for Patients With Early-Stage Papillary Thyroid Cancer

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ABSTRACT

Purpose
Decision-making on adjuvant radioactive iodine (RAI) treatment for early-stage papillary thyroid cancer (PTC) is complex because of uncertainties in medical evidence. Using a parallel, two-arm, randomized, controlled trial design, we examined the impact of a patient-directed computerized decision aid (DA) on the medical knowledge and decisional conflict in patients with early-stage PTC considering the choice of being treated with adjuvant RAI or not. The DA describes the rationale, possible risks and benefits, and the medical evidence uncertainty relating to the choice.

Patients and Methods
We recruited 74 patients with early-stage PTC after thyroidectomy. Participants were assigned by using 1:1 central computerized randomization to either the DA group with usual care (intervention) or usual care alone (control). Medical knowledge about PTC and RAI treatment (the primary outcome), as well as decisional conflict (a secondary outcome), were measured by using validated questionnaires, and the respective scores were compared between groups.

Results
Consistent with PTC epidemiology, 83.8% (62 of 74) of the participants were women, and the mean age was 45.8 years (range, 19 to 79 years). Medical knowledge about PTC and RAI treatment was significantly greater and decisional conflict was significantly reduced in the DA group compared with the control group (respective P values <.001). The use of adjuvant RAI treatment was not significantly different between groups (DA group, 11 of 37 [29.7%]; controls, seven of 37 [18.9%]; P = .278).

Conclusion
A computerized DA improves informed decision making in patients with early-stage PTC who are considering adjuvant RAI treatment. DAs are useful for patients facing decisions subject to medical evidence uncertainty.
For patients with early-stage PTC whose primary tumor is larger than 1 cm in diameter, the current expert recommendation is that most patients should undergo total thyroidectomy and that RAI treatment (also known as remnant ablation) be selectively considered.6-8 There is considerable uncertainty in the evidence-based medical literature regarding the possible long-term benefit of adjuvant RAI treatment in reducing the risk of thyroid cancer-related recurrence in patients with early-stage PTC.9 The uncertainty relating to adjuvant RAI treatment in early-stage PTC stems from the lack of long-term randomized controlled trials in this field and the conflicting findings of existing observational studies examining recurrence risk.9 Despite these limitations,9 RAI has been increasingly used in the treatment of thyroid cancer in the United States in recent decades.10 For example, in Americans younger than age 45 years who have been diagnosed with early-stage, well-differentiated thyroid cancer, the rate of use of adjuvant RAI treatment has increased from 3.3% of patients in 1973 to 38.1% in 2006.11

Although adjuvant RAI treatment is being increasingly used in thyroid cancer,11 some patients may lack an awareness of the uncertainties related to treatment benefit and possible risks and may desire detailed supplemental information.12 Decision aids (DAs) are instruments used to inform patients about available health care options, including evidence about potential treatment benefits and risks.13 They may improve patients’ medical knowledge,14,15 increase active participation in medical decision making,14 and reduce decisional conflict14 compared with usual care. It is not known how a DA that explains medical evidence uncertainty related to a cancer treatment might have an impact on patients’ medical knowledge and decisional conflict.

We recently developed and pilot-tested a patient-directed, computerized DA explaining the choice to accept or reject adjuvant RAI treatment for treatment of early-stage PTC.16-18 It is intended to be used as an adjunct to individualized physician counseling, and it explains the following topics relating to adjuvant RAI treatment decision making for early-stage PTC: disease prognosis (disease-related mortality and recurrence risks), rationale for or against the treatment, potential benefits of the treatment (including the potential to facilitate disease surveillance and some conflicting evidence on the impact of recurrence risk), potential short-term adverse effects associated with the treatment (such as fatigue, nausea/vomiting, neck pain, salivary gland swelling/pain, taste changes, and dry mouth), potential long-term risks of the treatment (such as dry mouth, nasolacrimal duct obstruction, impact on menses, and the risk of second primary malignancies), uncertainty of relevant medical evidence on treatment benefit, disease follow-up implications, and reproductive considerations.16-18 The data cited within the DA were based on a literature review, including some of our own published systematic reviews.9,19-21 Within the DA, we explicitly reported the uncertainty of medical evidence related to the use of adjuvant RAI treatment for early-stage PTC, including an account of the lack of randomized controlled trials in the field and the limitations in interpreting the best available observational evidence.

Our primary objective in this randomized controlled trial was to evaluate the impact of this DA on medical knowledge of patients with early-stage PTC. Secondary objectives were to examine the impact of the DA on patients’ decisional conflicts and the ultimate treatment choice.

**PATIENTS AND METHODS**

**Trial Design**

Consenting patients with early-stage PTC, for whom either accepting or declining adjuvant RAI treatment would be equally appropriate, were randomly assigned to a one-time exposure to a computerized DA (plus usual care) or to no exposure to a DA (with usual care), respectively. This parallel design randomized controlled trial was conducted in a single academic clinical center (Toronto General Hospital, University Health Network). The complete study protocol has been previously reported.22 This trial was registered with ClinicalTrials.gov, and it was approved by the University Health Network Research Ethics Board. All participants provided written, informed consent.

**Inclusion Criteria**

Potentially eligible patients included individuals aged 18 years or older who had complete surgical resection of their thyroid gland on or after September 1, 2009, and were diagnosed with early-stage (low-risk) PTC on the basis of a surgical pathology report review (ie, primary tumor size between 1 and 4 cm in diameter, with no known positive lymph nodes, no extension of the tumor outside the thyroid, no vascular or lymphatic invasion, and no known distant metastases, with no tall cell features [American Joint Committee on Cancer stage 1 or 2 in the absence of distant metastases]22). Participants were required to be able to communicate in spoken and written English, use a computer, and provide informed consent.

**Exclusion Criteria**

Individuals concurrently diagnosed with any medullary, anaplastic, or poorly differentiated (or de-differentiated) thyroid cancer or thyroid lymphoma or those who had already received RAI treatment for thyroid cancer were not eligible for this study. Individuals who temporarily stopped taking thyroid hormone (for RAI treatment or testing) were not eligible to participate in the study while not being given the medication, because of the possibility that this could have a negative impact on cognitive abilities. Individuals whose thyroid cancer pathologic stage could not be confirmed were also ineligible.

**Intervention**

All participants received their usual care and counseling from their respective treating physicians before and after random assignment. In our region, usual care typically involves the care of a specialized head and neck surgeon (otolaryngologist or general surgeon with expertise in thyroid surgery) as well as one or more medical specialists (such as an endocrinologist, radiation oncologist, or nuclear medicine physician). All of the surgical and medical specialists are qualified under the Royal College of Physicians and Surgeons of Canada and participate in an annual maintenance of certification program. We had no restriction in our study on the types or number of physicians involved in patients’ care. Participants in the intervention group self-navigated the DA Web site for up to a maximum of 60 minutes, on a personal desktop computer in a research office at the Toronto General Hospital. A research assistant supervised the study visit but was not allowed to navigate the DA or discuss medical content with the participant. To prevent contamination of the control group, no access to the DA Web site was permitted outside the study visit, and participants were not allowed to take home any materials that may have been printed from the Web site. Access to the DA Web site was password protected and only the study staff had access. No access to the DA was available to any physicians or patients outside the study during the trial. Participants were contacted by telephone approximately 6 to 12 months following random assignment to confirm their ultimate treatment choice.

**Outcomes**

The primary outcome of medical knowledge (measured by a questionnaire) was collected at the initial study visit, immediately after random assignment and exposure to the DA (in the intervention group), or without DA exposure (in the control group). The medical questionnaire was self-administered and consisted of 10 true or false questions (scored by number of correct responses out of 10, with a maximal score of 10).16,17 The medical knowledge questionnaire encompassed the following topics: early-stage PTC...
yet been assigned. There was no blinding of participants, study staff, or treating investigators, nor treating physicians were aware of the allocation, because it had not the random assignment/testing visit, neither the participant, study staff, investigators, nor treating physicians were aware of the allocation, because it had not yet been assigned. There was no blinding of participants, study staff, or treating physicians after random assignment was completed. However, the statistician was blinded to the allocation of groups at the time of data analysis.

**Random Assignment, Allocation Concealment, Implementation, and Blinding**

Central computerized randomization in a 1:1 ratio was performed at a patient level by using variable block sizes of 2 and 4 (allocation designed by a study statistician [K.E.T.]). After the participant signed informed consent for participation in the study, random assignment was performed by using the DA program, and the study allocation was then revealed to the participant. Immediately following random assignment, during the same study visit, intervention group participants were exposed to the DA (followed by testing), and the control group participants underwent testing (without DA exposure). Before the random assignment/testing visit, neither the participant, study staff, investigators, nor treating physicians were aware of the allocation, because it had not yet been assigned. There was no blinding of participants, study staff, or treating physicians after random assignment was completed. However, the statistician was blinded to the allocation of groups at the time of data analysis.

**Statistical Methods and Sample Size Considerations**

All analyses followed an intention-to-treat principle. For descriptive analyses, categorical data were expressed as number and percentage, whereas continuous data were expressed as mean and standard deviation (or range). Independent (Welsh’s) two-sample t tests were used to compare questionnaire scores (expressed as continuous data) from medical knowledge and decisional conflict questionnaires in the intervention group compared with the control group. A Pearson’s χ² analysis was used to perform a preplanned secondary analysis comparing the rate of RAI treatment use in each group at follow-up. The cutoff for statistical significance for all analyses was α = 0.05. Quantitative statistical analyses were performed by using PASW Statistics 18.0 (IBM, Chicago, IL) and R 2.12.0 (The R Foundation for Statistical Computing, Vienna, Austria).

The sample size was calculated to detect a one-point difference in the mean score of the knowledge questionnaire between the intervention and usual care groups, assuming a standard deviation of 1.5 (Power and Precision software; Biostat, Englewood, NJ). The intended sample size was 37 individuals per group (total of 74; two-tailed α = 0.05; power 0.808).

**RESULTS**

**Participant Characteristics**

The 74 study participants, including 62 women, were recruited between March 2010 and June 2011, and the study flow of participants is summarized in Figure 1. The characteristics of study participants are provided in Table 1. The mean time participants spent self-navigating the DA Web site was 30.1 minutes (standard
participants in the control group identified the following individual(s) as primarily responsible for the ultimate treatment decision: the patient, 24.3% (nine of 37); or shared decision between the patient and the physician, 51.4% (19 of 37).

Medical Knowledge, Decisional Conflict, and Treatment Choice

All data were complete, with no missing responses to questions. Medical knowledge about prognosis of early-stage PTC and adjuvant RAI treatment was significantly greater in the DA group (mean score, 9.7 of a maximum of 10; SD, 0.6; n = 37) compared with the control group (mean score, 7.8 of 10; SD, 1.3; n = 37; mean difference, 1.9; 95% CI, 1.4 to 2.3; P < .001). Decisional conflict relating to the decision to accept or reject adjuvant RAI treatment was significantly reduced in the DA group (mean score, 25.2 of a maximum score of 100; SD, 9.7 of 10; n = 37) compared with the control group (mean score, 36.9 of 100; SD, 21.9; n = 37; mean difference, 12.8; 95% CI, 18.4 to 35.3; P < .001). Furthermore, decisional conflict was reduced in all respective subscales of this tool in the DA group compared with the control group (respective P values < .001 for the Uncertainty Subscore, Informed Subscore, Values Clarity Subscore, Support Subscore, and Effective Decision Subscore). The treatment preferences of participants throughout the study and ultimate treatment choice are given in Table 2. The rates of use of adjuvant RAI treatment were not significantly different between the two groups (decision aid group, 11 of 37 [29.7%]; controls, seven of 37 [18.9%]; \( \chi^2 = 1.175; df = 1; P = .278 \)).

In this randomized controlled trial, we have shown that a computerized DA that explains the choice of receiving or not receiving adjuvant RAI treatment improves medical knowledge and reduces decisional conflict of patients with early-stage PTC. However, exposure to the DA does not appear to have a significant impact on the ultimate RAI treatment choice. These findings are in keeping with recent systematic reviews of DAs in the medical literature, suggesting that DAs may improve patients’ knowledge\(^14,15\) and reduce decisional conflict,\(^14,15\) but they may have variable effects on the choice of medical treatment.\(^14,15\) We believe that DAs may be particularly valuable in facilitating decision making on complex interventions for which there is some evidence uncertainty. We believe that sharing information about evidence uncertainty relating to the choice of cancer treatment may result in more informed choices by patients and more realistic treatment expectations. This view is compatible with the recent Salzburg Statement on Shared Decision Making in which a call was made for clinicians to share important decision making with patients and provide accurate information about options and uncertainties tailored to individual patients’ needs.\(^28\) It is important to understand that although most patients want to have information relevant to a medical treatment choice, patients’ individual preferences on the degree and nature of involvement in the final treatment decision may be highly variable,\(^28\) and this may partly explain the heterogeneous effects of DAs on ultimate treatment choice.

### Table 1. Participant Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Decision Aid Group (n = 37)</th>
<th>Control Group (n = 37)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No.</td>
<td>%</td>
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<tr>
<td>Female sex</td>
<td>31</td>
<td>83.8</td>
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<tr>
<td>Age, years</td>
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<td></td>
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<tr>
<td>Marital status</td>
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<tr>
<td>Single</td>
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<tr>
<td>Married or common law</td>
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<td>62.2</td>
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<td>Divorced or separated</td>
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<td>Highest education completed</td>
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<td>English as a first language</td>
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<td>Self-reported frequency of computer use</td>
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<tr>
<td>Most days</td>
<td>34</td>
<td>91.9</td>
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<td>Few times per week</td>
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<td>5.4</td>
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<tr>
<td>Once a week</td>
<td>1</td>
<td>2.7</td>
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<tr>
<td>AJCC(^{28}) pathologic stage*</td>
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<tr>
<td>1</td>
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<td>67.6</td>
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<tr>
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<td>Primary tumor size, cm</td>
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<tr>
<td>No. of months since completion of thyroidectomy</td>
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<td>1.8</td>
</tr>
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</table>

Abbreviations: AJCC, American Joint Committee on Cancer; SD, standard deviation.

*None of the patients had distant metastatic disease at primary diagnosis.
The strengths of this trial include the use of a randomized controlled design, review of surgical pathology reports (to ensure a homogenous thyroid cancer population), strict attention to avoiding external contamination of the control group (with no access permitted to the DA outside the study setting), and the completeness of data collection. Limitations of this study include a relatively small sample size, an uncertainty of the clinical significance of the measured differences in medical knowledge, a lack of measurement of thyroid hormone levels in study participants, a lack of data on the medical knowledge of treating physicians providing usual care, a lack of prospectively collected objective data on the interactions between study participants and their treating physicians (such as audio or video recordings of clinical discussions or measurements of clinical time used), and a lack of long-term outcome data on the effects of the DA (although collection of such data is planned in extended follow-up to our study). There are also several limitations that restrict the external generalizability of our results to other settings or populations, such as the performance of the study in one study center, the availability of the DA only in English, the relatively high education level and degree of computer experience of our study participants, the timing of the decision making (ie, a mean of a few months after thyroidectomy), and the exclusion of individuals who may have been withdrawn from the performance of the study in one study center, the availability of the DA only in English, the relatively high education level and degree of computer experience of our study participants, the timing of the decision making (ie, a mean of a few months after thyroidectomy), and the exclusion of individuals who may have been withdrawn from the decision making process and long-term health and psychosocial outcomes.

In conclusion, a computerized patient-directed DA significantly improves medical knowledge and reduces decisional conflict in patients with early-stage PTC who are considering adjuvant RAI treatment. Our data also suggest that DAs may facilitate knowledge translation for decisions on cancer treatment that are subject to uncertainty of medical evidence. More research is needed to determine whether DAs that focus on other choices for cancer treatment subject to similar medical evidence uncertainty can improve the decision-making process and long-term health and psychosocial outcomes.

The author(s) indicated no potential conflicts of interest.
REFERENCES

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