Treatment and Outcomes in Differentiated Thyroid Cancer: A Retrospective Exploration in Three UK Centres That Provide Different Advice on Low Iodine Diets

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Abstract

Background International guidelines on the treatment of differentiated thyroid cancers promote low iodine diets (LID) before radioiodine remnant ablation. Evidence that the LID ultimately improves treatment success is inconsistent. This study aimed to determine if there is a difference in ablation success rates according to provision of advice to follow a LID.

Methods Retrospective study of patients with differentiated thyroid cancer treated with total thyroidectomy and radioiodine remnant ablation between 01/01/2015 and 31/12/2016 in 3 centres advising: no LID (C1: n=108); LID for 1-week before (C2: n=50); LID for 2-weeks before and 48 hours (C3: n=59) after RRA. Response to treatment was determined by adapted American Thyroid Association Dynamic Risk Stratification Score, stratified as excellent, indeterminate, or incomplete response.

Results In total, 217 patients were included in the analysis. We found differences in preparation for radioiodine remnant ablation and in the assessment of outcomes between centres. Furthermore, although there was little difference in staging between centres there was a difference in the percentage of patients receiving 1.1GBq vs higher administered activities (15% in C1, 22% in C2 and 44% in C3, p<0.001). An excellent response was recorded for 49% in C1, 48% in C2 and 36% in C3 (p=0.61). With C1 as reference group, the odds ratios (OR) for an excellent response were C2 OR: 0.96 (95% CI 0.46,2.00) and C3 OR: 0.62 (95% CI 0.29,1.30), p=0.40.

Conclusions We found no evidence that advice to follow a low iodine diet for 1 or 2 weeks before radioiodine remnant ablation impacts on ablation success but differences between centres means the results should be regarded as exploratory. There is no immediate need to change practice regarding the LID, but a prospective multi-centre study with a more homogenous approach to patient management or a randomised controlled trial will provide more definitive recommendations.

Background

Globally, over 255,000 new cases of thyroid cancer were recorded in 2017, with 70% in women(1). A third of cases live in higher-income countries, but the age standardised incidence rate is increasing fastest in middle-income countries. In 2017 in the UK there were 1068 new cases of thyroid cancer in men and 2756 in women compared with 310 in men and 815 in women in 1993(2). Increasing incidence of thyroid cancer is a global trend, although mortality is, in most regions, falling(1).

Differentiated thyroid cancer (DTC) accounts for 95% of cases and has 10-year survival rates of 80–90%(3). DTC is usually treated with total thyroidectomy, which may be followed by treatment with radioactive iodine (^{131}I) to destroy residual thyroid or cancerous tissue. 'Radioiodine remnant ablation' (RRA) denotes destruction of residual thyroid tissue whereas 'radioiodine therapy' refers to ^{131}I administration for known residual local or metastatic disease(3). The decision on whether to proceed with ^{131}I, and the administered activity, is determined, in part, by staging and histological features. Depending on these factors, patients are classified into three groups 1) definite indications for RRA (large tumour size or extensive extra thyroidal extension or distant metastases) 2) uncertain indications 3) no indication (small tumour size, no extra thyroidal extension, minimally invasive, well-differentiated). The decision to proceed or not is individualised for patients in group 2, taking into account

factors such as tumour size, histology, lymph node involvement and full extent of any extra thyroidal extension and after discussion of risks and benefits of RRA with the patient(3).

Thyroid stimulating hormone (TSH) is raised to facilitate uptake of ^{131}I. This used to be achieved through thyroid hormone withdrawal (THW) but, since approval in the mid-2000s, recombinant human TSH (rhTSH) is routinely used(4). Non-radioactive iodine competes with ^{131}I for uptake, which may reduce efficacy of RRA(5). In relation to iodine status at the time of RRA, the European Association of Nuclear Medicine Therapy Committee recommends aiming for a urine iodine concentration (UIC) of < 100mcg/l and postponing RRA if UIC > 150-200mcg/l(5). International guidelines state that iodinated contrast agents should be avoided in the 8 weeks before RRA, to avoid RRA if amiodarone has been taken within the previous 12 months and, based on expert opinion, recommend a low iodine diet (LID) for 1 to 2 weeks prior to RRA(3–6). LID advice reduces iodine intake and iodine status in patients with high iodine intake(7, 8). However, no randomised controlled trials have been conducted on whether LIDs improve ablation success, and evidence from cohort and retrospective studies is mixed(9, 10), particularly in countries with low dietary iodine, such as the UK(11).

Despite acknowledging the lack of evidence for LIDs, British Thyroid Association guidelines advise an LID prior to RRA(3). In the UK, many treatment centres use the UK Low Iodine Diet Working Group diet sheet and advise restricting fish, seafood, seaweed, dairy produce, eggs, iodised salt (although salt is not routinely iodised in the UK) and a wide variety of foods containing these ingredients as well as nutritional supplements and cough mixture(12). However, different treatment centres give differing advice, particularly regarding length of dietary restriction and when to restart usual diet(13). The effect of LID advice on treatment success in the UK has not been examined.

This is a retrospective study of patients with DTC comparing response to RRA in three UK centres that give different LID advice prior to RRA. The aim is to determine if there is a difference in response according to provision of advice to follow a LID.

Methods

Sites

We recruited three UK treatment centres that routinely administer RRA for thyroid cancer giving different LID advice. Centre 1 (C1) did not advise patients to follow a LID, Centre 2 (C2) advised a LID for one week prior to RRA and Centre 3 (C3) advised a LID for two weeks prior to RRA and 48 hours post.

Patients

Clinical records of patients diagnosed with DTC who underwent RRA for thyroid cancer at the three sites between 01/01/2015 and 31/12/2016 were reviewed. Eligible patients were those treated with one stage or two stage total thyroidectomy and diagnosed with papillary or follicular thyroid cancer by histology. Included patients were those with stages N0 to N1b and treated with any administered activity who had been prepared with either rhTSH or THW protocol. Records were excluded if patients had distant metastases, were experiencing recurrence, or had two radioiodine therapies planned from the outset due to residual disease or local involvement of surrounding tissue. Patients diagnosed during 2016 but treated with RRA during 2017 were excluded. Identification of thyroid cancer during treatment for other cancers was not an exclusion criterion.

Outcome

Response to treatment was determined by a three tier system advised by UK Guidelines for the Management of Thyroid Cancer(3), adapted from the American Thyroid Association Dynamic Risk Stratification Score (ATA Score)(14) which uses results from neck ultrasound (US) and thyroglobulin (Tg) tests at 9 to 12 months post ablation. Responses are classified as excellent response (low risk of recurrence), indeterminate response (intermediate risk of recurrence) and incomplete response (high risk of recurrence). Where neck US was not available, results from diagnostic whole-body scan (DxWBS) was used(3). Thyroglobulin is secreted by normal and cancerous thyroid cells and detectable Tg post-thyroidectomy indicates remnant thyroid tissue or the presence of residual or recurrent tumour(3). Tg may be measured using immunometric assays (Tg-IA) or radioimmunoassays (Tg-RIA). Tg antibodies (TgAb) can interfere with the measurement of Tg, producing falsely low results and masking disease. Both Tg-IA and Tg-RIA are subject to false negatives, but no TgAb detection cut-off exists that eliminates false negatives and false positives(15). Patients with no evidence of disease on neck US or DxWBS, supressed or stimulated Tg < 1ug/l and any detectable TgAb were classified as an indeterminate response, in strict accordance with the ATA Score.

Data extraction

Anonymised data on demographics, details of surgery, tumour, node and metastasis (TNM) staging, ^{131}I dose, post ablation assessment and evaluation of treatment success at 9 to 12 months post RRA were extracted. Data extraction was undertaken and checked by clinical staff or trained coders.

Statistical analysis

Overall comparisons were made between centres with respect to patients' ages, gender, grouped TNM stage (7th edition)(16), ^{131}I administered activity, and ATA Score, using chi-squared tests or one-way ANOVA as appropriate. These were followed by within-centre comparisons of these variables between patients with excellent, indeterminate, or incomplete outcomes.

Across all centres, numbers of people experiencing an incomplete response were small so indeterminate/incomplete responses were combined. The main analysis used logistic regression to compare centres in respect of excellent response, adjusting successively for age and sex and then administered activity of ^{131}I and TNM stage; coding for response was incomplete/indeterminate = 0 vs excellent = 1, therefore higher odds were associated with better outcomes. A sensitivity analysis was undertaken with a graded response, using ordered logistic regression (proportional odds), coding the response as incomplete = 1, indeterminate = 2, excellent = 3. For both the main analysis and sensitivity analysis C1 was the comparison group.

Results

A total of 289 records were screened, 217 were eligible (C1 = 108, C2 = 50, C3 = 59). Distant metastasis (n = 30 [42%]) and recurrence (n = 18 [25%]) were the most common reasons for ineligibility. Differences were observed between centres regarding preparation for RRA and tests used to assess treatment success. C2 and C3 prepared patients using rhTSH, assessed success with neck US and measured Tg using Beckman Tg-IA for all cases(17). In contrast only 9 patients in C1 were assessed through neck US and Tg-IA measures (Roche E170). However, C3 was less likely to use supressed Tg measures than C1 and C2. These differences were unexpected and the initial objective to determine if there was a difference in treatment success according to provision of LID advice was

hampered by this. The results provided below are therefore considered exploratory in nature, and any differences observed between centres may not be due to differences in LID advice.

Descriptive comparison between centres

Table 1 shows between-centre comparisons in respect of age, gender, TNM stage, ^{131}I administered activity and the results of post ablation whole body scans (PaWBS). C1 had fewer patients with TNM stages III/IV than the other centres, but there was little statistical evidence of a difference between centres ($p = 0.14$). A difference was observed between ^{131}I administered activity above 1.1GBq; fewer patients in C3 received higher activities ($P < 0.001$). PaWBS indicated that four (4%) patients in C1 and four (7%) in C3 showed uptake in cervical nodes. Within-centre differences in response failed to show overall differences between subgroups (except possibly for C3 (TNM stage and administered activity), but numbers were small) (Supplementary tables).

Table 1
– Between centre comparisons of patient and tumour characteristics and response to treatment

Centre	Centre 1 (Col. %)	Centre 2 (Col. %)	Centre 3 (Col. %)	p-value (Chi-squared unless indicated)
Total patients	108	50	59	-
Age at diagnosis (years)				
Mean (SD)	*50.0 (15.3)*	*44.5 (15.0)*	*49.7 (17.7)*	*0.12*[1]
≤45	42 (41%)	27 (54%)	26 (44%)	0.32
>45	60 (59%)	23 (46%)	33 (56%)	
Sex				
Male	37 (34%)	17 (34%)	18 (31%)	0.88
Female	71 (66%)	33 (66%)	41 (70%)	
TNM stage				
I/II	66 (73%)	30 (60%)	34 (60%)	0.14
III/IV	24 (27%)	20 (40%)	23 (40%)	
Administered activity ^{131}I (GBq)				
1.1	16 (15%)	11 (22%)	26 (44%)	< 0.001[2]
3.7	89 (82%)	39 (78%)	33 (56%)	
5.5	2 (2%)	0 (0%)	0 (0%)	
7.4	1 (1%)	0 (0%)	0 (0%)	
Post ablation whole body scan				
Uptake in neck (unspecified or in keeping with residual thyroid tissue)	97 (90%)	41 (82%)	52 (88%)	0.001
No uptake	0	0	2 (3%)	
Uptake in cervical nodes	4 (4%)	0	4 (7%)	

Centre 1 = no low iodine diet (LID) advice; Centre 2 = 1 week LID advice; Centre 3 = 2 week LID advice and 48 hours after ablation

ATA = American Thyroid Association; Col % = column percentage; LID = low iodine diet; SD = standard deviation; TgAb = thyroglobulin antibodies; TNM = cancer staging (tumour, node, metastasis)

[1]*means compared with one-way ANOVA*

[2]*administered activity 1.1 vs ≥ 3.7Gbq in Centre 1 to facilitate chi-squared analysis*

[3]*complete responders vs combined Indeterminate/Incomplete*

Centre	Centre 1 (Col. %)	Centre 2 (Col. %)	Centre 3 (Col. %)	p-value (Chi-squared unless indicated)
Other / unclear	3 (3%)	7 (14%)	0	
ATA score				
Excellent response	52 (49%)	24 (48%)	21 (36%)	0.61
Indeterminate	45 (43%)	22 (44%)	31 (53%)	*(0.26[3])*
Incomplete	9 (9%)	4 (8%)	6 (10%)	
Centre 1 = no low iodine diet (LID) advice; Centre 2 = 1 week LID advice; Centre 3 = 2 week LID advice and 48 hours after ablation				
ATA = American Thyroid Association; Col % = column percentage; LID = low iodine diet; SD = standard deviation; TgAb = thyroglobulin antibodies; TNM = cancer staging (tumour, node, metastasis)				
[1]means compared with one-way ANOVA				
[2]administered activity 1.1 vs ≥ 3.7Gbq in Centre 1 to facilitate chi-squared analysis				
[3]complete responders vs combined Indeterminate/Incomplete				

Differences in response

Centre differences in response are shown in Table 2. Although the response at C3 appeared worse than at other centres, the confidence intervals around the odds ratio (OR) were wide and there was no good evidence for a difference between centres, with or without adjustment for known confounders, i.e., age, gender, and TNM stage and activity of ^{131}I (C2 OR: 0.96 (95% CI 0.46,2.00); C3 OR: 0.62 (95% CI 0.29,1.30), p = 0.40). The sensitivity analysis, with graded response, showed similar results (C2 OR: 0.96 (95% CI 0.47,1.95); C3 OR 0.64 (95% CI 0.32,1.30).

Table 2
– Logistic regression to compare centres in respect of excellent response (vs combined indeterminate/incomplete)* assessed using the ATA Score

Centre (overall % with excellent response, n = 214)	**Unadjusted** **N = 214**	**Minimally adjusted** ***(age** and sex)*** **N = 208**	**Partially adjusted** ***(age, sex, dose*** of ^{131}I)*** **N = 208**	**Partially adjusted** ***(age, sex,*** ***TNM stage)*** **N = 194**	**Fully adjusted** ***(age, sex,*** ***TNM stage and dose of*** ^{131}I***)*** **N = 194**
	OR (95% CI)	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**
Centre 1 (49%)	1 (Ref.)	1 (Ref.)	1 (Ref.)	1 (Ref.)	1 (Ref.)
Centre 2 (48%)	0.96 (0.49,1.88)	1.01 (0.50,2.02)	1.03 (0.51,2.08)	0.92 (0.45,1.91)	0.96 (0.46,2.00)
Centre 3 (36%)	0.59 (0.31,1.14)	0.60 (0.31,1.16)	0.66 (0.33,1.33)	0.56 (0.28,1.14)	0.62 (0.29,1.30)
Overall p-value****	0.26	0.26	0.45	0.25	0.40
Centre 1 = no low iodine diet (LID) advice; Centre 2 = 1 week LID advice; Centre 3 = 2 week LID advice and 48 hours after ablation					
Ref = reference group					
*coding for response in this analysis incomplete/indeterminate = 0, excellent = 1, therefore higher odds indicate more favourable outcome					
**Continuous					
***5.5Gbq and 7.4Gbq combined					
****Likelihood-ratio test					

Discussion

This retrospective study of patients with DTC compared treatment response rates at 9 to 12 months post RRA from three centres in the UK that gave different LID advice prior to RRA. We found differences between centres in both preparation and determination of treatment success, which was not expected at the outset of this study. Comparison between centres was thus hampered, and findings should be treated as exploratory.

We found no evidence for a difference in ablation success at 9 to 12 months assessment between the centres, adjusting for age, sex, TNM stage and administered activity ^{131}I. Treatment response for C3 (2-week LID) appeared worse, with a 40% reduction in the odds of experiencing an excellent response compared to that of experiencing an excellent response at C1 (no LID). However, the confidence interval was wide and included no difference and when an outcome is common the odds ratio will tend to overestimate underlying risk. There was no difference in effect size between C1 (no LID advice) and C2 (1-week LID).

Only 45% of included patients were classified as experiencing an excellent response at 9 to 12 months post RRA, which appears low. Ablation success was determined using the ATA Score combining results of neck US or DxWBS with stimulated or supressed Tg measurements(3). Patients with TgAb were not removed from the analysis but, in accordance with the guidelines, were classified as having an 'indeterminate' response. However, results from DxWBS or neck US alone indicate that no abnormality was detected for 84% of patients (data not shown), which is comparable with success rates reported in other studies, including the Hi Lo trial(18).

Comparison with other LID studies

No randomised controlled trials have examined whether LID advice prior to RRA or radioiodine therapy improves treatment success rates in thyroid cancer. In 1983 Maxon et al(19) observed that use of a LID increased ^{131}I administered activity to the tumour during diagnostic scans (LID = 19 vs normal diet = 21), but evidence that the LID improved treatment success was lacking. Since then, retrospective examinations of patient records have been conducted to determine whether use of LID improves success rates or whether iodine status is associated with treatment success. Table 3 summarises relevant studies. Only Pluijmen et al(20) found that there was a difference in success rates between patients advised to follow a LID and those who were not. However, between studies there is variation in preparation, ^{131}I administered activity, how response to treatment is assessed and whether patients with detectable TgAb were excluded or not.

Table 3
– Summary of studies examining the impact of low iodine dietary advice or iodine status on radioiodine therapy success rates

Author, year, country	Study design	Preparation; administered activity	Comparisons	Iodine status at radioiodine therapy	Treatment success (% successful)	Comments
Morris et al, 2001 USA	Retrospective comparison of cohorts treated between 1990–1994 vs 1997–1999 Total n = 92	THW 3.7GBq or 5.5GBq	LID advice for 10–14 days prior to RRA. Less stringent LID (avoid fish, seafood and iodine supplements) (n = 50) Stringent LID (n = 42)	Less stringent LID (n = 7 healthy volunteers) vs Stringent LID (n = 7) Mean (sd) UIC 381 (196) mcg/L vs 174 (128) mcg/L	Assessed by DxWBS alone Less stringent LID vs Stringent LID **62% vs 68%, p = 0.53**	Higher success rates were observed at higher administered activity in both groups. Although more patients in the stringent LID group were treated with 3.7GBq than 5.5GBq, subgroup sample sizes were too small to provide evidence that the LID improved success rates at lower doses.
Pluijmen et al, 2003 Netherlands	Retrospective comparison of cohorts treated between 1986–1991 vs 1992–1998 Total n = 120 Excluding patients with TgAbs	THW 2.9GBq	No LID advice (n = 61) LID for 4 days prior to RRA, only patients with 24-UIE < 50mcg/day included (n = 59)	No LID advice (n = 9) vs LID advice (n = 59) Mean (sd) 24-UIE 159 (9.0) mcg/day vs 27 (11.6) mcg/day	Assessed by DxWBS plus Tg No LID vs LID **48% vs 65% p < 0.001**	A LID that reduces iodine status to < 50mcg/day improves efficacy radioiodine therapy.
Tala Jury et al, 2010 Italy	Retrospective cohort treated between 1998–2008	rhTSH (n = 76) THW (n = 125)	No specific LID advice, patients advised to avoid iodine containing drugs or supplements for 2 weeks prior to RRA	Mean UIC (n = 201) 132 (160) mcg/L	Assessed by DxWBS alone (n = 201)	No difference in mean UIC between those who were successful and those who were not for either

DxWBS = Diagnostic whole body scan; LID = Low iodine diet; n = number; OR = Odds ratio; RRA = Radioiodine remnant ablation; rhTSH = Recombinant human thyroid stimulating hormone; Tg = Thyroglobulin; TgAb = Thyroglobulin antibodies; THW = thyroid hormone withdrawal; sd = Standard deviation; UIC = Urine iodine concentration; UI/Cr = Urine iodine creatinine ratio; UIE = Urine iodine excretion

Author, year, country	Study design	Preparation; administered activity	Comparisons	Iodine status at radioiodine therapy	Treatment success (% successful)	Comments
						definition of success. No difference between rhTSH and THW for success rates or mean UIC.
	Total n = 201	1.1GBq to 5.5GBq			**85% success for total group**	
					Stratified by UIC	
					(mcg/L) < 50 (n = 41) 88% 50–100 (n = 54) 82% 101–150 (n = 47) 81% 151–200 (n = 25) 85% 200–250 (n = 17) 88% > 250 (n = 17) 82%	
					Assessed by DxWBS plus Tg, excluding	

DxWBS = Diagnostic whole body scan; LID = Low iodine diet; n = number; OR = Odds ratio; RRA = Radioiodine remnant ablation; rhTSH = Recombinant human thyroid stimulating hormone; Tg = Thyroglobulin; TgAb = Thyroglobulin antibodies; THW = thyroid hormone withdrawal; sd = Standard deviation; UIC = Urine iodine concentration; UI/Cr = Urine iodine creatinine ratio; UIE = Urine iodine excretion

Author, year, country	Study design	Preparation; administered activity	Comparisons	Iodine status at radioiodine therapy	Treatment success (% successful)	Comments
					patients with TgAbs (n = 81) **61.7% successful**	
Yoo et al, 2011 South Korea	Retrospective comparison of cohorts treated between 2004–2005 vs 2006–2007 Total n = 161	THW 5.5GBq	LID advice for at least 14 days prior to RRA Less strict LID (n = 71) Strict LID (n = 90)	Not measured	Assessed by DxWBS plus Tg and TgAb Less strict LID vs strict LID **80.3% vs 75.6%, p = 0.475**	No difference in success rates between the two groups

DxWBS = Diagnostic whole body scan; LID = Low iodine diet; n = number; OR = Odds ratio; RRA = Radioiodine remnant ablation; rhTSH = Recombinant human thyroid stimulating hormone; Tg = Thyroglobulin; TgAb = Thyroglobulin antibodies; THW = thyroid hormone withdrawal; sd = Standard deviation; UIC = Urine iodine concentration; UI/Cr = Urine iodine creatinine ratio; UIE = Urine iodine excretion

Author, year, country	Study design	Preparation; administered activity	Comparisons	Iodine status at radioiodine therapy	Treatment success (% successful)	Comments
Sohn et al, 2013 South Korea	Retrospective cohort treated between Feb 2009-June 2010 Total n = 295 Excluding patients with TgAbs	THW 1.1GBq	Strict LID for 14 days prior to RRA No comparison	Mean (sd) UI/Cr 88.7 (192.3) mcg/gCr	Assessed by DxWBS alone **80.3% success for total group** Assessed by DxWBS plus Tg, **75% success for total group** Urine iodine level (µg/gCr) < 50 (n = 205) 82% 50–100 (n = 54) 83.3% 100–250 (n = 16) 87.5% 250 (n = 20) 50%	When patients were stratified into four groups by iodine status, only UIC > 250mcg/gCr (n = 20) was associated with treatment failure (OR 3.88, 95% CI 1.42 to 10.57).

DxWBS = Diagnostic whole body scan; LID = Low iodine diet; n = number; OR = Odds ratio; RRA = Radioiodine remnant ablation; rhTSH = Recombinant human thyroid stimulating hormone; Tg = Thyroglobulin; TgAb = Thyroglobulin antibodies; THW = thyroid hormone withdrawal; sd = Standard deviation; UIC = Urine iodine concentration; UI/Cr = Urine iodine creatinine ratio; UIE = Urine iodine excretion

Iodine status

Only two studies(21, 22) summarised in Table 3 measured iodine status in all participants. Sohn et al(22) reported a reduction in success rates only in people with very high iodine status, although Tala Jury et al(21) did

not observe a similar reduction. Non-randomised(7, 8, 23, 24) and randomised(25, 26) studies have shown that advice to follow an LID for one to two weeks can lower UIC to < 100mcg/l. However, iodine status is not routinely measured prior to RRA in the UK(13) and we were unable to assess whether patients reduced their iodine status or whether iodine status itself was associated with treatment success. It is also unknown whether patients in C1 reduced high iodine foods despite being given no specific LID advice. There is readily available information on-line about the LID(27) which patients could have accessed. We have conducted qualitative work that suggests patients not given advice to follow a LID may still reduce iodine intake(28).

Other strengths and limitations

This is the first study conducted in the UK to investigate whether advice to follow a LID prior to RRA affects treatment success in DTC. Ideally, the only difference in treatment across centres would have been in the dietary advice given. However, unexpectedly, there was evidence for a difference between the centres in ^{131}I administered activity with fewer patients in C3 having higher administered activity. The fully adjusted model corrected for activity but there were also differences in preparation and assessment methods between centres that we were not aware of when designing the study. Although we do not consider these to be factors that would substantially affect treatment success(29), this meant we were not comparing identical practices. Given that evidence from other studies seems to indicate that following a LID prior to RRA does not confer substantial benefits in terms of outcomes, the differences between centres may have masked any small benefits from a LID.

Recommendations for research and practice

This study forms part of a larger overall project examining advice to follow a LID prior to ablation. We have conducted a qualitative study investigating the impact of the advice on patients(28) and a survey of practice regarding the use of the LID in the UK(13). This retrospective study indicates that routinely collected data cannot be used in the UK to determine whether advice to follow an LID has an impact on treatment success due to centre-level differences on top of differences in LID advice. In the UK, it is unclear whether current LID advice successfully lowers iodine intake or iodine status and, globally, it remains unclear as to whether low iodine status improves treatment success. The flaws in our retrospective study indicate that there is a need for an RCT or, given that the LID is widely used in clinical practice, a large well-controlled prospective observational study to determine 1) whether LID advice lowers iodine status and 2) whether lowering iodine status has an impact on treatment success rates.

Conclusion

We conducted this retrospective review to determine if following a low iodine diet for 1 or 2 weeks prior to RRA for differentiated thyroid cancer contributed to treatment success. In common with other retrospective studies, we found no evidence that such advice impacted on success rate. However, differences in preparation and assessment meant we were not comparing identical practices across centres and the results should be treated as exploratory. There is no immediate need to change practice regarding the LID in the centres giving different dietary advice, but there is a need for greater harmonisation in overall treatment, drawing on evidence from recent trials(30). We believe that adequately powered well-controlled prospective studies and, potentially, an RCT, are required to confirm the role of a LID prior to RRA on the outcomes of treatment.

List Of Abbreviations

ATA = American Thyroid Association

95% CI = 95% Confidence interval

DTC = Differentiated thyroid cancer

DxWBS = Diagnostic whole-body scan

LID = Low iodine diet

OR = Odd ratio

PaWBS = Post ablation whole body scan

RCT = Randomised controlled trial

rhTSH = Recombinant human thyroid stimulating hormone

RRA = Radioiodine remnant ablation

Tg = Thyroglobulin

TgAb =Thyroglobulin antibodies

Tg-IA = Thyroglobulin immunometric assays

Tg-RIA =Thyroglobulin radioimmunoassays

THW = Thyroid hormone withdrawal

TSH = Thyroid stimulating hormone

UIC = Urine iodine concentration

UI/Cr = Urine iodine creatinine ratio

UIE = Urine iodine excretion

US = ultrasound

Declarations

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Not applicable

Ethical approval and consent statement

The UK National Health Service Health Research Authority (https://www.hra.nhs.uk/) which oversees the research ethics process within the UK, advised that, according to national regulations, this study was a Clinical Surveillance Audit and did not need a review by a Research Ethics Committee. The study was formally approved locally as a Service Evaluation by The Royal Liverpool and Broadgreen University Hospital Trust, Liverpool, England and as an Audit by University Hospital Bristol and Weston NHS Trust, Bristol, England and by Velindre University NHS Trust, Cardiff, Wales and, as such, information officers and audit mangers at each Trust determined that consent to participate was not needed on the basis that the study used anonymised data. Administrative permissions to extract anonymised clinical data used in the study was granted by each Trust to local staff with substantive or honorary contracts.

Consent for publication

Not applicable

Availability of data

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interest statement

IHS is the lead and LM is a member of the UK Low Iodine Diet Working Group. The remaining authors have nothing to declare.

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Author contributions

CE, MB, LM, SV, IHS, GM, GH, AN and CA designed the study; CE and GH undertook literature research. Data extraction was performed by CE, MB, LM, IHS, SV and GM. Statistical analysis was conducted by KIH and LH under supervision of SL. CE drafted the initial manuscript which was revised and edited by all authors.

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