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A survey of UK centres on low iodine diet recommendations prior to radioiodine ablation therapy for differentiated thyroid cancer

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Abstract

Background: Guidelines suggest that a low iodine diet (LID) is advised prior to radioiodine ablation (RIA) for thyroid cancer. We aim to describe current practice regarding LID advice in the UK, determine uptake of the 2016 UK LID Working Group diet sheet and discover whether there are differences in practice. **Methods:** Online survey distributed between November 2018-April 2019 to centres in the UK that administer ¹³¹I. We asked questions on whether a LID is advised, for how long, how advice is presented, whether and how compliance is measured and whether treatment is delayed if LID advice is not followed. **Results:** Fifty-six clinicians from 47 centres that carry out RIA for thyroid cancer responded. Forty-four centres (94%) advise a LID prior to RIA, the majority for 14 days (82%). Two-thirds of centres use the UK LID Working Group diet sheet. Patients are told to resume normal eating when ¹³¹I is administered at 17 (39%) centres, with 18 (41%) advising waiting for 24-48 hours after administration. Most centres (95%) use only a simple question or do not assess compliance. Only 2 (5%) indicate that RIA would be delayed if someone said they had not followed LID advice. **Conclusions:** UK practice regarding the LID prior to RIA for thyroid cancer is consistent with current guidelines but non-adherence does not usually delay RIA. The UK Low Iodine Diet Working Group diet sheet is widely recognised and used. Practice could be improved by centres working to harmonise advice on when to restart a normal diet.

250 words

1 Background

2 Thyroid cancer accounts for less than 1% of cancer cases in the UK. However, incidence is increasing
3 and between 2014 to 2016 there were an average of 3527 new cases of thyroid cancer annually in the
4 UK, compared to 1125 in 1993(1, 2). Differentiated thyroid cancer accounts for 95% of cases. The
5 prognosis for differentiated thyroid cancer is good, 10-year survival rate is 80-90%, although
6 recurrence or persistent disease is estimated to occur in 10-30% of cases(3), with rates as high as 68%
7 observed in high risk patients(4). Treatment is often total thyroidectomy, followed by radioiodine
8 remnant ablation with ¹³¹I (RIA) to destroy thyroid tissue remaining post-surgery(5). High iodine status
9 can interfere with uptake of ¹³¹I. The UK Guidelines for the management of thyroid cancer state that,
10 based on expert opinion, exposure to iodinated contrast and treatment with drugs or supplements
11 high in iodine should be avoided, and people should be advised to follow a low iodine diet (LID) of 1-
12 2 weeks, prior to RIA(5). There is, however, mixed evidence on whether LIDs impact on ablation
13 success(6), particularly in countries with generally low iodine intakes such as the UK(7).

14 Two reviews have been conducted, one systematic(8), one narrative(6), examining the use of LIDs
15 prior to RIA. Randomised controlled trials indicate that advice to follow a LID for 1-2 weeks reduces
16 urinary iodine. However, evidence that LID advice improves ablation success comes only from
17 retrospective studies and is inconclusive. A study in the Netherlands(9) compared people who
18 followed a LID for 7-days and reduced 24-hour urinary iodine excretion to <50mcg/day with historic
19 controls given no dietary advice. Those following a LID experienced 65% success rate vs 48% for
20 controls (p<0.001). A study in Korea(10) found only excessive iodine intake, measured as a urinary
21 iodine creatinine ratio (UI/Cr) >250mcg/gCr, to be associated with increased odds of unsuccessful
22 ablation (OR: 4.74, 95% CI: 1.78–12.63). Three other retrospective studies, in the USA(11) and
23 Korea(12, 13) have found no difference in ablation success rates between cohorts that were advised
24 a 10-14 day LID and historic controls who were given no advice(11); no difference between people
25 following a very restrictive 2-week LID vs those following a less restrictive 2-week LID(12); and no
26 difference in either ablation success or spot urine iodine concentration (UIC) between people
27 following a 1-week vs those following a 2-week LID(13).

28 Despite the mixed evidence, the European Association of Nuclear Medicine Therapy Committee
29 recommends that RIA should be postponed if UIC is >150-200mcg/l(3) and that clinicians should aim
30 for a UIC <100mcg/l or a UI/Cr of <100mcg/gCr, with optional LID advice. UK guidelines do not give
31 details on the level of iodine restriction necessary to achieve a UI/Cr of <100mcg/gCr, whereas
32 American Thyroid Association guidelines advise restricting iodine intake to <50mcg/day(6). In
33 contrast, in Korea, where intakes of iodine are much higher than in the UK and USA, guidelines are to
34 restrict iodine intake to <100mcg/d. Italian guidelines do not advise an LID at all prior to RIA(14).

35 In the 2000s, there were anecdotal reports in the UK that there were variations in practice and patients
36 were finding LID advice confusing(15). Consequently, the UK Low Iodine Diet Working Group (UK LID-
37 WG) developed a UK LID diet sheet(16) and initially distributed it in 2016 (supplement). It is uncertain
38 how widespread use of the diet sheet is and, given the lack of robust evidence that a LID affects
39 ablation success and that international guidelines differ, it is possible that practice within the UK still
40 varies.

41 This study was a survey of current practice regarding advice on LIDs prior to RIA in the UK. The aims
42 were to determine whether practice varies across different centres, whether the UK LID-WG diet sheet
43 is in use (and if not, why not) and to discover whether centres monitor compliance with a LID and if
44 treatment is delayed if a LID is not followed.

45 **Methods**

46 A short electronic survey was designed on Online Surveys (Jisc, UK) for distribution to centres in the
47 UK that administer ¹³¹I for people undergoing treatment for thyroid cancer. The survey included 10
48 main questions, with a maximum of 20 follow-ups. Questions were a mixture of multiple choice with
49 some free text boxes and included questions on how well clinicians thought patients coped with the
50 diet (supplement). The survey could be completed anonymously, although at the end people were
51 asked to identify their centre. Participation in the survey was voluntary, with informed consent
52 assumed through completion.

53 There is no national list of centres that administer radioiodine in the UK. A list of possible centres was
54 created from information held by the UK LID-WG, the Internal Dosimetry Users Group and through
55 the authors' clinical networks. A brief invitation e-mail containing a link to the questionnaire and an
56 explanation of the purpose of the survey was sent to identified centres in November 2018 and up to
57 three reminders were sent between January 2019-April 2019. Practice regarding who prescribes and
58 administers RIA varies in the UK, so e-mail addresses of clinicians known personally to the authors or
59 listed on hospital websites were used or e-mails were sent to Nuclear Medicine or radiology
60 department addresses. The e-mail included the contact details of two of the authors (CE and LM) so
61 that recipients could find out more details or request no further contact. Information and a link to the
62 survey was also distributed at a Thyroid Cancer Study day held at the Royal Marsden Hospital, London
63 in December 2018. In April 2019 follow up e-mails were sent to hospitals in regions that appeared to
64 have low coverage.

65 Responses were collated and are presented descriptively. Qualitative free text responses were
66 summarised.

67 **Results**

68 Sixty-four hospitals were contacted, and responses were received from 53 (83%). Six hospitals (9%)
69 indicated that they were not centres for RIA for thyroid cancer. Clinicians from 47 centres
70 administering RIA (73%) completed the survey. For seven centres two responses were received and
71 for one centre there were three responses, giving a total of 56 responses. Overall, national coverage
72 was good (table 1). Responses were received from radiologists and nuclear medicine specialists
73 (physicists and nurses) (n=15), other clinical nurse specialists (n=12), clinical scientists (n=12),
74 oncologists (n=8), nuclear medicine consultants (n=3), unspecified consultants (n=4), one
75 endocrinologist and one dietitian.

76 The mean estimated number of people treated with radioiodine for thyroid cancer at each centre/year
77 was 46 (SD 28), giving a total estimated number of people treated of 2182 annually. The minimum
78 number treated per centre was estimated to be 10 people, the maximum 150.

79 Three centres did not routinely advise a LID prior to RIA for all people. Of these, one small centre
80 (treating approximately 10 people/year) indicated that they were not aware of the guidelines and
81 another (treating approximately 80 people/year) indicated that there was no evidence for
82 effectiveness. The remaining centre (treating approximately 40 people/year) responded that the
83 provision of LID advice varied by clinician and it was more common not to advise the diet. Another
84 centre also indicated that advice to follow a LID varied by clinician, one centre advised a LID for only
85 2 days prior to RIA, all others advised restriction for 1-2 weeks, as per the guidelines.

86 Table 2 summarises survey answers from the 44 centres who indicated that they advised people to
87 follow a LID. For some questionnaire items, different responses were provided by different clinicians
88 from the same centre, indicated in the table.

89 Most centres (66%) reported using the UK LID-WG diet sheet. Of those who did not, four (9%) were
90 not aware of the working group suggestions and clinicians from four centres (9%) thought it was too
91 restrictive, one of whom specifically said they did not advise people to restrict dairy products as much.

92 People were instructed to resume a normal diet immediately after taking ¹³¹I at 17 (39%) centres, 2
93 hours after taking the RIA capsule by one centre and 24-48 hours after taking the capsule at 18 (41%)
94 centres. Six centres indicated that people were instructed to resume a normal diet 24-48 hours after
95 treatment, but a LID inpatient menu was not provided. Compliance with the LID advice was assessed
96 in 26 (59%) centres, although all except one used a simple verbal check rather than a formal dietary
97 assessment. None of the centres reported measuring iodine status and only two clinicians said their
98 centre would delay treatment if someone said they had not followed a LID.

99 Thirty-one of the 56 clinicians (53%) indicated that they thought people coped very well with the diet,
100 although free text comments indicated that some groups of people were more likely to find the diet
101 difficult, specifically, people with diabetes, vegans/vegetarians, older people and people from non-
102 British backgrounds. The diet was identified as being a source of anxiety for some people, and there
103 were comments that some people were more restrictive than advised and attempted to follow no-
104 iodine diets, rather than reduced iodine. However, clinicians also said that there were people who
105 liked feeling in control of a part of their cancer treatment, and who experienced other health benefits
106 from thinking about what they were eating. The UK LID-WG diet sheet was highlighted as making
107 advice clearer and easier to follow.

108 Two clinicians (a clinical nurse specialist and an oncologist) thought that people did not cope with the
109 diet but provided no specific comments, and one oncologist reported not asking about the diet
110 because they didn't think there was good evidence for efficacy so it didn't matter if people followed
111 it or not.

112 **Discussion**

113 This study gives information about clinical practice regarding low iodine diets prior to RIA for thyroid
114 cancer in the UK since the introduction of the UK LID-WG diet sheet(16). The response rate was good
115 with very good coverage across the regions of the UK, including all the devolved nations. Most centres
116 advise a 14-day LID but there were variations regarding the advice given between centres. Overall,
117 there was good awareness and usage of the UK LID-WG diet sheet and only four centres indicated that
118 they were unaware of it. A further four said that they disagreed with some of the information in the
119 sheet.

120 Variations in practice are perhaps unsurprising given the lack of clear evidence that following a LID or
121 reducing UIC improves ablation success(6, 8). Of the four centres that reported not routinely advising
122 a LID, only one large centre explicitly stated that they did not think the evidence was good enough.
123 However, adherence to the diet was either not assessed at all or assessed by a simple question by
124 most clinicians and only two indicated that treatment would be delayed if people reported that they
125 did not follow a LID. This may reflect either a widespread lack of belief that the diet is necessary, as
126 stated by one clinician, or a lack of confidence in ability to assess diet. None of the centres assessed
127 iodine status using urinary iodine measurements, again perhaps unsurprising given concerns over
128 inaccuracies in determining iodine status from UIC(17).

129 There appears to be most disagreement in practice about when people should restart a normal diet
130 following RIA. Twenty-five of the 56 clinicians who answered the survey reported that they advised
131 people to continue with dietary restriction 24-48 hours after RIA and six indicated that the LID was
132 stopped after post-therapy whole body scan (Px-WBS), presumably to ensure good uptake of ¹³¹I.
133 Although we did not ask each centre to report when the Px-WBS occurred, it is carried out when
134 residual activity permits imaging, typically around 2-10 days after RIA(5). Studies that examine
135 whether advice to follow a LID improves ablation success report asking people to follow a LID prior to
136 RIA but did not appear to ask people to continue after ¹³¹I has been administered(9-11, 13), unless a
137 Px-WBS was carried out(12). To our knowledge, no studies have assessed whether continuing a LID
138 beyond the administration of RIA confers any benefit on outcomes, or what effect resuming a usual
139 diet has on iodine status in this immediate post-treatment period.

140 As a survey of practice, our study did not capture what patients think of the LID. Over half of clinicians
141 (53%) indicated that people coped very well with the diet, although some suggested that there are
142 groups of people who struggle and that some people attempt to follow a very restrictive no-iodine
143 diet. Two studies, both conducted in Korea, reported that people believed the LID to be important but
144 found it difficult to follow because they enjoyed foods high in iodine, struggled to find alternatives
145 and found it difficult to eat outside the home(18, 19). Difficulties with food eaten outside of the home
146 were also reported by people in Brazil(20). Experiences may be different in the UK since the typical
147 Korean diet is very high in iodine(21) and, in Brazil salt is iodized(20). However, there was anecdotal
148 evidence that people in the UK found LID advice confusing and difficult to follow before the UK LID-
149 WG released the standardised diet sheet(15). Clinicians in the current survey indicated that the
150 standardised diet sheet has improved advice, but questions from people about the LID are still
151 frequently posted on on-line forums(22).This is perhaps because there is potential for confusion if
152 people find on-line advice from countries where salt is iodized (e.g., the USA) unlike the UK.

153 This study is the most comprehensive overview of UK practice regarding advice on the LID prior to RIA
154 for thyroid cancer to date but there are some limitations. Despite good coverage, it is likely that not
155 all UK centres have taken part. It is also possible that the clinician who completed the survey may not
156 have been the one who knew most about practice regarding the LID in their centre, despite the initial
157 recipient being asked to forward it to a more appropriate person if they felt they were unable to
158 answer the questions. Overall, however, we are confident that this study is broadly representative of
159 current UK practice regarding LID advice prior to RIA therapy for thyroid cancer.

160 We found evidence that the UK LID-WG diet sheet is recognised, used and has improved practice.
161 Most UK practice regarding the LID is in line with current guidelines but there are variations between
162 centres and non-adherence to the diet does not usually delay RIA. This is, perhaps, due to lack of
163 convincing evidence in the literature that the LID is necessary. There is a need for more research in
164 this area and this study is a part of an ongoing work investigating the LID. We are currently conducting
165 a multi-centre retrospective review of ablation success rates between UK centres giving different LID
166 advice, a qualitative study exploring patient experiences with the LID and a mixed- methods review of
167 the literature regarding the LID prior to RIA for thyroid cancer. However, since LID advice is widely
168 given at present, UK practice could be improved with more detailed assessment of dietary compliance,
169 and harmonisation of advice on when to restart a normal diet.

170 **2491 words**

171

172 **Statements**

173

174 **Acknowledgment**

175 We would like to thank all the clinicians who completed the survey.

176 **Statement of ethics**

177 Ethical approval was not required to conduct the study.

178 **Disclosure statement**

179 LM and IHS are members of the UK Low Iodine Diet Working Group. The remaining authors report
180 no conflict of interest.

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185 **Author contributions**

186 The study was conceived by all the authors. CE, GH and IHS drafted the survey which was tested and
187 refined by all the other authors. CA, MB, CE, IHS and LM researched and finalised the list of sites and
188 disseminated the survey. CE and CA analysed the results and CE wrote the first draft of the paper,
189 which was commented upon by all other authors.

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253

254 **Tables**

255 Table 1. Regional responses

256 Table 2. Summary of survey answers for 44 centres advising a low iodine diet prior to radioiodine
257 ablation.

258 Supplement: UK Low Iodine Diet Sheet; UK Low Iodine Diet Working Group Supporting Documents;
259 survey items and possible response options