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The impact of the extent of thyroid resection complemented by radioiodine management on disease free status and discharge rates among differentiated thyroid cancer patients: A retrospective analysis

Mpumelelo Nyathi, Nyebe Phineas Mahlangu

Dr George Mukhari Academic Hospital, Sefako Makgatho Health Sciences University, Ga-Rankuwa, South Africa

RESEARCH

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Corresponding Author:
Mpumelelo Nyathi
Dr George Mukhari Academic Hospital,
Sefako Makgatho Health Sciences University, Ga-Rankuwa, South Africa
Email: Mpumelelo.Nyathi@smu.ac.za

ABSTRACT

Background

Well-differentiated thyroid cancers (DTC) are common endocrine cancers. They originate from follicular cells and parafollicular cells, and they have good prognosis. The pivotal treatment is surgery followed by radioiodine management. However, the extent of thyroid resection remains debatable. Currently both total thyroidectomy (TT) and thyroid lobectomy (TL) are performed followed by radioiodine management.

Aims

The study aimed at evaluating the impact of the extent of thyroid resection complemented by radioiodine management on disease free status and discharge rates among DTC patients.

Methods

A retrospective analysis of DTC patients' files managed with radioiodine post-surgery in the Department of Nuclear Medicine at Dr George Mukhari Academic Hospital. The information extracted from the patient files included; the patient's gender, histology, age, diagnosis, the nature of surgery (TT or TL), date of ablation, quantity of radioiodine dose administered and patients' treatment status.

Results

Sixteen patients met the study criteria; having had thyroid resection and later managed with radioiodine. A total of 5/16 (31.3 per cent) patients underwent TL and 11/16 (68.7 per cent) underwent TT. At the end of the study period, 5/11 (45.5 per cent) TT patients had been discharged compared to 1/5 (20 per cent) TL patients. The study also established that TL patients received higher cumulative doses compared to TT patients during the treatment, despite only two TL patients having been diagnosed with metastasis.

Conclusion

Administration of radioiodine among TT patients increases disease free status while among TL patients its role is debatable. TT optimises the management DTC with radioiodine resulting in improved outcomes.

Key Words

Total thyroidectomy, thyroid lobectomy, nuclear medicine, radioiodine, well-differentiated thyroid cancers

What this study adds:

1. What is known about this subject?

Surgery is definitive first line treatment of DTC usually followed by radioiodine management to treat metastasis and to ablate remnant tissues.

2. What new information is offered in this study?

Management of TT patients with radioiodine improves the disease free status whereas its role among TL patients is debatable.

3. What are the implications for research, policy, or practice?

Management of TL patients with radioiodine should be done on case by case individual basis after a careful assessment of clinical, histology, molecular and biochemical data.

Background

Thyroid cancer is the most common of all endocrine cancers. Most of these cancers are well-differentiated hence they are called well-differentiated thyroid cancers (DTC). Majority of them are either papillary or follicular carcinomas. Both papillary and follicular carcinomas originate from follicular cells and they have good prognosis.[1] Surgery is an established first line treatment usually followed by radioiodine treatment.[2,3] Radioiodine has for years been used as a treatment option post-surgery.[4] It is available in form of sodium iodide capsules thus facilitating easy administration,[5] post-surgery.[6,7] Administration of radioiodine saves two purposes; ablation and treatment hence we use of the terms radioiodine ablation and radioiodine treatment in management of DTC patients.[8]

Radioiodine treatment is aimed at post-operative or metastatic residual disease.[9,10] A full body scan is usually acquired 2–5 days after administration of the treatment from which the presence of distant metastases can be detected. The main advantage of this scan is its sensitivity when compared to diagnostic scans since it is acquired using high dose.[4]

Radioiodine ablation is normally achieved with the first dose administered post total thyroidectomy.[4,8] It is aimed at destroying the subclinical, microscopic foci of the remaining unknown cancerous tissues in the thyroid bed,[7-9] lymph nodes and other sites.[9,10] Radioiodine ablation is also aimed at preventing recurrences.[9] However, the extent of thyroid resection remains debatable. Some clinicians are of the view that only total or near total thyroidectomy should be performed,[7,8] while others feel that partial thyroidectomy or lobectomy can still be performed.[9] Lack of high quality data hinders the support of either of the two management decisions. This leaves room for use of either thyroid lobectomy or total thyroidectomy. However, limited thyroid lobectomy is preferred in Japan with limited use of radioiodine,[11] while in the western countries, their guidelines accept both procedures followed by radioiodine management albeit on individual assessment.[12,13]

The study aimed at evaluating the impact of the extent of thyroid resection complemented by radioiodine management on disease free status and discharge rates among DTC patients.

Method

A retrospective analysis of 51 DTC files of patients managed with radioiodine post-surgery from 2007–2013 in the Department of Nuclear Medicine at Dr George Mukhari Academic Hospital, Ga-Rankuwa, South Africa. The information extracted from the patients' files who satisfied the selection criteria included; the patient's gender, histology, age, diagnosis, the nature of surgery (TT or TL), date of ablation, quantity of radioiodine dose administered and patients' treatment status.

Results

Sixteen out of fifty one patients satisfied the study criteria. Eleven of these patients underwent TT while five underwent TL. By end of the study period, 5/11 (45.5 per cent) were declared disease free after being managed with radioiodine compared to 1/5 (20 per cent) of TL patients (Tables 1 and 2). An individual analysis of administered cumulative doses showed that TL patients were administered with more cumulative radioiodine dose compared to TT patients despite only 2/5 TL patients having been diagnosed with metastases.

Lastly, the study established that the failure to comply with treatment schedules resulted in patients staying longer under treatment as was the case with the patients SSHA, MMUL and SNKU (Table 2). Furthermore, all TL lobectomy patients whose pre-ablation showed no evidence of metastasis were found to have developed secondary cancers on follow up thus keeping them longer under treatment. Among the detected secondary cancers were the lung- mediastinum, and female breast cancers.

Discussion

Well-differentiated thyroid cancers, unlike other types of cancers, increase during adolescence and early adult life. In the United States of America (USA), the increase is observed up to the age 45 years, declining at over 75 years. The increase in DTC incidences maybe attributed to environmental factors.[14] However, there is another view that attributes increases in disease incidence to improvements in radiological diagnostic techniques,[15] such as the high resolution ultrasound modality which are capable of detecting microcarcinomas which were previously not detected.[16] DTC has good prognosis and the survival rates can be as high as 90 per cent.[17] However, what constitutes effective management of DTC remains

controversial despite the agreement that surgery is the most effective first line treatment.

A controversy exists on the choice of total thyroidectomy over unilateral lobectomy.[15] Harmer and McCready,[18] favoured near total or total thyroidectomy in conjunction with excision of the adjacent lymph nodes when involved followed by radioiodine treatment specifically for metastases. However, the American Thyroid Association (ATA) recommends that low-risk patients undergo thyroidectomy while patients with tumours >1cm should undergo total thyroidectomy,[13] followed by radioiodine management. Middendorp et al.,[3] proposed that the extent of surgery or thyroid resection should be dependent of the accurate stratification of DTC. However, stratification is not well defined. On the other hand, the Japanese guidelines prescribe limited thyroidectomy as they prefer lobectomy.[11] In this retrospective study, we established that total thyroidectomy has better disease free outcomes when compared to thyroid lobectomy.

Among the five thyroid lobectomy patients managed with radioiodine from January 2007 to December 2013 (Table 1), only one patient 1/5 (20 per cent) was declared disease free and discharged by end of study period. However, during the same period, 5/11 (45 per cent) total thyroidectomy patients managed with radioiodine were declared disease free and discharged (Table 2). These findings take us one step closer to supporting total thyroidectomy over thyroid lobectomy as a first line treatment of option of DTC patients since the study results established that more TT patients compared to TL patients were declared disease free.

A further analysis of Tables 1 and 2 shows that both groups of patients (TT and TL) were managed with radioiodine post-surgery. The management of the two groups with radioiodine was in line with worldwide standard protocols,[12,13] with the exception of Japanese guidelines that emphasise selective use of radioiodine for high risks patients.[11] Of interest in this retrospective study was that 3/5 (60 per cent) of the thyroid lobectomy patients were managed with radioiodine despite not having any evidence of manifestation of the metastasis in their pre-ablation scan. A possible explanation of this approach could be that managing the thyroid lobectomy patients with radioiodine was aimed at preventing future recurrences. Furthermore, initial administration of radioiodine might have been aimed at facilitating disease follow up. However, the decision to manage TL patients with radioiodine is delicate in addition to being complex in the sense that radioiodine is a source of secondary cancers.

Diez et al.[18] proposed use of small dose, 30mCi, in the event the physicians desired to follow up of the disease. This quantity of radioiodine dose gave similar results as that achieved with higher doses. However, in this retrospective study, the initial doses administered post-surgery to patients who did not have any evidence of metastasis were 80mCi, 100mCi and 150mCi. Based on these quantities of radioiodine administered, it may be conclude that the physician may have prescribed these two doses with either of the two objectives; to treat any remaining or unknown disease in the thyroid remnant and lymph nodes with the view of preventing future recurrences and to facilitate future follow up of the disease. If the second objective was the reasoning of the physician then the administered doses were too high, as it has been previously established by Diez et al.,[8] that 30mCi equally facilitates disease follow up just like high doses. Administering high radioiodine on DTC patients' post-surgery is associated with further complications. According to Kruiff et al.,[19] high radioiodine dose makes patients prone to secondary cancers and it puts female patients at a higher risk of developing these secondary cancers. These observations were in agreement with the findings of the current study. The three TL female patients identified as A, C and E had pre-ablation scans that did not show any evidence of metastasis before management with radioiodine. However, follow up scans showed that some had developed secondary cancers in the breasts, lungs and mediastinum. These results were not unique for this study. Rubino et al.,[20] also established that as much as 27 per cent of TL patients managed with radioiodine dose of 100mCi risked developing secondary cancers. According to these authors, there exists a linear dose-response relationship between radioiodine and tumour appearance.

Verkooijen et al.,[21] also reported elevated risks of development of breast secondary cancers post radioiodine therapy. However, the limited statistics in this study, that is 3/3 (100 per cent) of TL cases who apparently developed secondary cancers might be alarming. This should be viewed as a limitation attributed to the small sample of patients. However our view point still stands based on the findings by other researchers whose results were based on larger samples. In the light of our findings and those of other researchers,[20,21] it is also worth taking into account the views of the British Thyroid Association with regards to management of DTC patients with radioiodine. They do not recommend use of radioiodine in cases where patients had carcinomas <1cm that do not show high risks features.[12] On the other hand the American Thyroid Association guidelines recommend selective use of radioiodine.[13] Selective use of

radioiodine when managing thyroid lobectomy patients is essential in order to avoid the long term side effects of the treatment as well as over-treatment. A decision to prescribe radioiodine should therefore be based on careful assessment of the following data; histology, molecular and biochemical and clinical. In this study, TL female patients were found to be more prone to secondary cases post management with radioiodine, an observation previously established by Kruiff et al.[19]

The TT patients identified as RMPE; EMTH; MKGA; HMOT and DDLA (Table 2) were declared disease free and discharged by the end of the study period, thus accounting for up to 5/8 (62.5 percent) discharge rate of TT patients without metastases compared to a discharge rate of 1/3 (33.3 per cent) of TL patients who did not have evidence of metastases prior to being managed with radioiodine. This high discharge rate among TT patients compared to TL patients takes us to a conclusion that TT optimizes patients for radioiodine treatment/management. These findings are in agreement with guidelines from western countries,[12,13] which recommend radioiodine management post total thyroidectomy as the best procedure to achieve high disease free outcomes. Historically, radioiodine is administered to treat any remaining, unknown disease in the thyroid remnant, lymph nodes and other locations and to prevent recurrences.[7] In this study, the above historical objective was achieved since discharge rates and disease free outcomes achieved among TT patients were indeed high at 62.5 per cent (62.5 per cent).

Lastly the study also established that non-compliance with radioiodine treatment prolonged the time to discharge. All the total thyroidectomy patients 3/11 (27.2 per cent) who for one reason or other missed treatment, remained on treatment at the end of the study period. However, all the TT patients with no metastasis had been discharged by the end of the study period and had less accumulative doses compared to TL patients.

Conclusion

The extent of thyroid resection plays a significant role in the duration of treatment of DTC patients managed with radioiodine. TT optimizes patients for radioiodine management thus resulting in more disease free outcomes compared to TL patients.

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PEER REVIEW

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CONFLICTS OF INTEREST

The authors declare that they have no competing interests.

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ETHICS COMMITTEE APPROVAL

The study was approved by Medunsa research ethics committee. The certificate number is MREC/M/68/2014:PG.

Table 1: TL Patients managed with I-131 post Lobectomy surgery

*Patient ID	Gender	Age	Subtype of DTC	Nature of surgery and date	Date of Referral to	Initial Date of management	Pre-ablation	Metastasis	Date & Individual Doses Administered	Compliance with	Status of Treatment
A	F	48	Papillary Carcinoma	Thyroid Lobectomy (Nov 2006) Completion Thyroidectomy 21/06/2007	23-03-2007	03-05-2007	Yes	No metastases 6/11/2008	3 x DOSES 3/05/07 -80 3/12/07- 100 23/06/08- 121 Cumulative Dose **301**	Yes	Discharged
B	F	66	Papillary Carcinoma	Thyroid Lobectomy 5/11/2009	25-11-2009	07-12-2009	Yes	Metastases in the lung and the liver 26-11-2009	5 x DOSES 07/12/09-100 12/07/11- 100 13/02/12- 150 04/09/12- 100 29/04/13- 100 Cumulative Dose **550**	Yes	Still On
C	F	47	Follicular Carcinoma	Lobectomy (Lt) (October 2010)	19-04-2010	06-06-2012	Yes	No metastases 30-05-2011	6 x DOSES 06/06/11- 100 05/12/11- 150 11/06/12- 100 11/12/12-150 02/07/13- 100 Cumulative Dose **600**	Yes	Still On
D	M	46	Follicular Carcinoma	Thyroid Lobectomy (Date not recorded)	01-04-2011	09-05-2011	Yes	Abnormal uptake in the chest 11-03-2011	3 x DOSES 09/05/11-200 08/11/11- 200 20/06/12- 100 Cumulative Dose **500**	Yes	Still On

E	F	48	Poorly Insular Differentiated Carcinoma	Thyroid Lobectomy 26/01/2012	30/01/2012	28/03/2012	Yes	No metastases 27/012/2012	3 x DOSES 28/03/12- 150 31/10/12- 200 03/07/13- 150 Cumulative Dose **500**	Yes	Still On

Table 2: Differentiated thyroid Cancer (DTC) Patients managed with radioiodine post total thyroidectomy

*Patient ID	Gender	Age	Subtype of DTC	Nature of Surgery and Date of Surgery	Date of Referral to the DNM	Initial Date of management	Pre-ablation scan done	Metastasis	Date & Individual Doses (mCi)	Compliance with treatment	Treatment Status
SSHA	F	41	Follicular	Total thyroidectomy 2003	21-08-2006	01-07-2008	Yes	No evidence suggestive of metastases 21-10-2008	5 x DOSES 1/07/08- 150 24/03/09- 150 9/03/11- 100 31/10/11- 100 21/05/12- 100 Cumulative Dose **600**	No	Still On
SNKU	F	57	Papillary	Total Thyroidectomy (3 Apr 2007)	14-03-2007	22-10-2007	Yes	Abnormal uptake on the right lung *Suspected metastases 21-09-2007	5 x DOSES 22/10/07- 100 22/07/08- 128 20/04/09- 150 17/11/09- 150 18/02/13- 100 Cumulative Dose **628**	No	Still On
RMPE	F	36	Follicular/ Papillary	Total thyroidectomy (Jan 2007)	04-06-2007	05-06-2007	No	No evidence suggestive of metastases 06-05-2008	4 x DOSES 5/06/07 -125 11/12/07- 76 8/07/08- 150 02/11/09-150 Cumulative Dose **501**	Yes	Discharged

RNGO	F	47	Follicular	Total Thyroidectomy (Apr 2008)	12-02-2009	24-11-2009	Yes	Metastases in the mediastinum 12-01-2009	1 x DOSE 24/11/2009-**100**	No	Still On
EMTH	F	59	Follicular	Total thyroidectomy (5/12/2008)	15-02-2009	30-03-2009	Yes	No evidence suggestive of metastases 25-03-2009	1 x DOSE 30/03/09- **150**	Yes	Discharged
MKGA	F	69	Hurthle Cell	Total thyroidectomy (17 Sep 2008)	10-03-2009	08-02-2010	Yes	No metastases 09-08-2011	1 x DOSE 8/02/10 -**100**	Yes	Discharged
DDLA	F	46	Follicular	Total thyroidectomy (March 2009)	17-02-2010	24-02-2010	Yes	No metastases 18-05-2010	1 x DOSE 24/02/10- **100**	Yes	Discharged
MMUL	M	38	Papillary	Total thyroidectomy (Nov 2011)	16-02-2011	07-03-2011	Yes	No evidence of metastases 05-10-2011	4 x DOSES 7/03/11- 100 7/11/11- 100 11/06/12-90 15/05/13- 100 Cumulative Dose **390**	No	Still On
HMOT	F	30	Papillary	Total thyroidectomy (Sept 2010)	25-02-2011	09-05-2011	Yes	No evidence of metastases 08-12-2011	1x DOSE 9/5/11- 150	Yes	Discharged
TMAK	F	47	Follicular	Total thyroidectomy (July 2011)	24-08-2012	15-10-2012	Yes	Metastases on the left upper chest 26-02-2013	2 x DOSES 15/10/12- 100 24/06/13- 100 Cumulative Dose **200**	Yes	Still On
LMOK	M	62	Papillary	Total thyroidectomy (Nov 2012)	21-02-2013	13-03-2013	Yes	No evidence of metastases 06-03-2013	1 x DOSE 13/03/13 -**100**	Yes	Still On