RESEARCH ARTICLE

Multinodular goitre surgery complications and directly observed surgeons' skills: A prospective double-blind observational cohort study

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Abstract

Objective: To study multinodular goitre patients' surgery by direct observation of surgical technique, and to compare complications with surgeons' skills and experience, for improved training of future thyroid surgeons.

Methods: Based on positivist epistemology and analytical observational design, this prospective double-blind study of a cohort of multinodular goitre patients operated upon by variedly experienced surgeons, was conducted at Bahawal Victoria Hospital Bahawalpur and Nishtar Medical University Hospital Multan, Pakistan, from December 2016 to April 2019. Patients were admitted through outpatient department and operated upon in routine operation lists. The surgeons were specialists/senior registrars, assistant professors, associate professors and professors. The patients were divided into two virtual groups: the one operated upon by surgeons with >3 years of post-fellowship experience and the other operated upon by surgeons with <3 years of post-fellowship experience. Surgeries were directly observed and differences in surgical technique and complications were recorded for respective groups. Data was analysed using SPSS 20.

Results: Of the 134 patients, there were 73(54.5%) in group 1 and 61(45.5%) in group 2. Overall, there were 119(88.8%) females and 15(11.2%) males. The overall mean age was 37.17±13.41 years (range: 14-80 years). Of the 25 surgeons, 13(52%) were in group 1 and 12(48%) in group 2. Group 1 had fewer complications compared to group 2, which on certain parameters was statistically significant ($p<0.05$).

Conclusion: Surgeons' experience and technique were found to have significant relationship with the rate of complications. Direct observation of surgeries is significant for real life evaluation and training of junior surgeons.

Keywords: Multinodular goitre, Complications of total thyroidectomy, Surgeons' experience in thyroid surgery.
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Introduction

Emil Theodor Kocher received Nobel Prize in 1909 for his pioneering work in understanding thyroid physiology. He, jointly with Theodor Bilroth, established thyroid clinics in Europe and proved safety in thyroid surgery through skilled surgical techniques.[1] Thyroid gland is divided by thin fibrous septae into lobules each composed of 20-40 follicles lined by cuboidal or low columnar epithelium and filled with thyroglobulin. Follicular epithelial cells, under the influence of hypothalamic factor and thyrotropin of anterior pituitary convert thyroglobulin into thyroxin (T4) and lesser amount of tri-iodothyronine (T3).[2]

Multinodular goitre is the most common among the disorders of thyroid gland.[3] Even in non-endemic regions, it is clinically detected in about 4% of adults beyond the age of 30. Worldwide, the most common cause of goitre is iodine deficiency. It has been estimated that goitres affect as many as 200 million out of 800 million people who have a diet deficient in iodine.[4] The World Health organization (WHO) recommends for adults the daily iodine intake of 150 micg which corresponds to a median urinary iodine concentration of 100 mcg/l.[5] Iodine deficiency and there-by increased stimulus of TSH results in thyroid follicular hyperplasia and colloid goitre. Then varying stimulus due to fluctuating levels of TSH results in nodular degeneration, haemorrhage and fibrosis leading to development of MNG. Multinodular goitre can be functionally normal (euthyroid), or it can be toxic due to over production of T3 and T4. Almost 25% cases of thyrotoxicosis are due to toxic multinodular goitre in which a long standing nontoxic goitre develops one or more hyperactive nodules that function independent of TSH levels.[6]

As not all individuals in the same iodine deficient region develop goitre, and as iodine supplementation does not prevent goitre development in all treated patients, and frequent occurrence of the disease in patients not exposed to iodine deficiency, other etiological factors are considered likely to be involved. Family studies have shown that children of parents with goitre have a significantly higher incidence of goitre than children of healthy parents. Hence fundamental process of goitrogenesis is independent of iodine deficiency but operates through mechanisms innate to hereditary and

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acquired heterogeneity among the thyrocytes themselves. Follicular cells are polyclonal both in structure and function and acquire new cellular qualities that become inheritable.[7] Thus hereditary has a part in the development of multinodular toxic and euthyroid goitre, toxic and euthyroid adenomas.

Nontoxic goitre appearing early in life suggests strong genetic susceptibility whereas environmental determinants are more likely to have additive or triggering effect. A genome-wide linkage analysis has identified a candidate locus MNG1 on chromosome 14q 31 in a large Canadian family with 18 affected individuals and also in a German family with recurrent euthyroid goiters.[8] Genes that code the proteins involved in thyroid hormone synthesis such as thyroglobulin gene (TG gene), thyroid peroxidase gene (TPO gene), the sodium iodide gene (SLC 5A5), the pendred syndrome gene (SLC 26 A 4), TSH-receptor gene (TSH-R gene), the iodotyrosine deiodenase gene (DEHL 1) and the thyroid oxidase 2 gene (THOX2) are candidate genes in familial euthyroid goitre. An abnormal three dimensional structure of TG was identified due to two different missense mutations in TG gene.[9] In addition to genetic predisposition, secondary factors involved in the development of MNG are goitrogens in Soy products and Vegetables of brassica family. Isoflavones especially genistein in soy and Isothiocyanates in brassica vegetables block TPO enzyme involved in the creation of thyroid hormone from iodide.

The treatment options in a patient of multinodular goitre (Figure-1) depend on the goitre size, compressive symptoms, age of patient, wish to maintain normal thyroid function, ability of gland to take up I^{131} and the risk of malignancy. Radioactive iodine therapy for non-

Figure-1: Multinodular goitre.

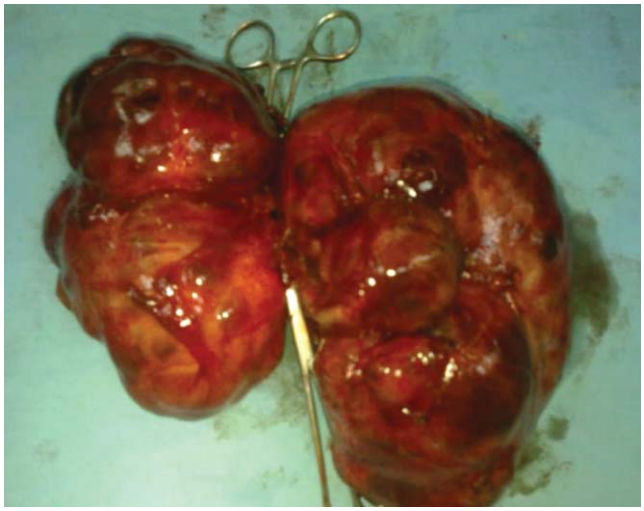

Figure-2: Surgical specimen: Total thyroidectomy.

toxic goitres is a reasonable therapeutic option in patients who are elderly or have contraindications to surgery.[10] The efficacy of radioactive iodine is proportional to its absorbed dose which in turn depends on goitre volume and functional status. Therefore, in goitre with less than 20% radioactive iodine uptake, conventional I^{131} therapy is not recommended.[11] In these cases recombinant human TSH is used before the administration of I^{131}, to increase its uptake by the thyroid gland.

Total thyroidectomy is the treatment of choice in multinodular goitre surgery (Figure-2). It is defined as removal of all visible thyroid tissue leaving behind viable parathyroid glands, intact recurrent laryngeal nerve (RLN) and external branch of superior laryngeal nerve. Near total thyroidectomy is defined by leaving less than 1gm of thyroid tissue adjacent to recurrent laryngeal nerve at the ligament of Berry on one side. Preservation of RLN and protection of parathyroid glands is achieved best by 'capsular dissection' which was first described by Halsted. Coller and Boyden in 1937, emphasised preservation the of external branch of superior laryngeal nerve by ligating the branches of superior thyroid artery individually.[12] Through these historical developments and understanding the variations in anatomy, thyroid surgery has evolved to the present day effectiveness and safety.

The aim of this study was to find the multinodular goitre surgery complications in our teaching hospitals' set-up, and map them against directly observed surgeons' skills as well as surgeons' experience.

Patients and Methods

The prospective double-blind study was conducted at Bahawal Victoria Hospital (BVH), Bahawalpur, and Nishtar Medical University Hospital (NMUH), Multan, Pakistan,

from December 2016 to April 2019. The ontology and epistemology of the research was based on positivism which assumes that facts can be collected and projected in realistic and objective manner. The positivist researcher takes on the role of independent observer who is impartial to the study findings and reports them objectively, using them to make informed decisions and recommendations.[13]

Basing on this positivist approach we adopted the analytical observational study design and got ethical approval of research initially from department with 'minimal disclosure' to avoid hawthorn effect. Post-hoc approval with complete disclosure was obtained from the institutional ethical review board of Quaid-E-Azam Medical College Bahawalpur.

The study population comprised a cohort of 134 patients with multinodular goitre (MNG) who were admitted through outpatient department (OPD) on 'first come first served' basis. They were diagnosed by clinical examination and/or ultra sound scan, thyroid hormone profile and radionuclide scan as and when required. They were euthyroid or their toxicity had been controlled with antithyroid drugs. The patients having single lobe disease, malignant disease, or recurrent disease, were excluded from the study.

All the patients were operated upon in general surgery operation theatres (OTs) on routine elective operation lists of respective surgical units. Patients were operated upon in one of the three OTs with no choice to be operated upon by a specific surgeon and similarly no choice for a surgeon to operate upon a particular patient. Hence there was no selection bias and the level of difficulty in surgeries was randomly distributed among surgeons. Patients and surgeons both were unaware or blinded to the research. After surgery the patients were shifted to general surgery ward where they were observed till discharge from hospital. Regarding post-surgery complications (Table-2), these patients were followed in surgical ward, in ICU, surgical HDU and in OPD clinics.

For observation and analysis the patients were placed into two virtual groups: group 1 having 73 patients who were operated upon by surgeons with >3 years post-fellowship experience; and group 2 having 61 patients operated upon by surgeons with <3 years post-fellowship experience. All the surgeons in both the groups were fellows in general surgery. The observational data was collected by directly observing the surgical technique of surgeons during routine operation theatre duties of the researchers who were not actively involved in surgeries included in the study. The operating technique of 25 surgeons was directly observed regarding dissection, ligation of upper pole vessels, identification of recurrent laryngeal nerve (RLN), skills of safeguarding the nerves, parathyroid glands and securing haemostasis. The differences in surgical technique of the two virtual groups of surgeons, were directly observed and recorded by taking 'field notes' in two column format (Table-3).

The complications of surgery recorded were: haematoma, hoarseness of voice due to transient or permanent RLN damage, low pitched voice due to suture entrapment of external branch of superior laryngeal nerve (EBSLN), and transient hypocalcaemia identified clinically and confirmed by serum calcium less than 8.0 mg/dl measured at two different occasions and 24 hours after surgery. Hypocalcaemia resulted from ischaemic damage to the parathyroid glands or poor identification and inadvertent removal during dissection and ligation of inferior pole vessels. RLN injury was confirmed by vocal cord dysfunction detected by laryngoscopy immediately after surgery, or by hoarseness of voice in later postoperative period. The EBSLN injury was labelled when weak low pitched voice was present on discharge from hospital. The nerve injury and hypoparathyroidism were considered permanent when the corresponding defect was present six months after surgery. Tracheostomy was recorded as an event/complication. The factors leading to tracheostomy were identified as surgery in huge long-standing goitre, tracheomalacia, and haematoma formation/anticipation.

All the data was recorded manually on paper and processed in 'MS Office Word-2007. For statistical analysis the data was processed in SPSS version 20. Fisher's Exact test was used to calculate the statistical significance in the rate of complications by the two groups of surgeons. $P<0.05$ was considered significant.

Results

Of the 134 patients, there were 73(54.5%) in group 1 and 61(45.5%) in group 2. Overall, there were 119(88.8%) females and 15(11.2%) males. The overall mean age was 37.17±13.41 years (range: 14-80 years). There were 105(78.35%) patients with euthyroid MNG and 29(21.64%) with toxic MNG. Total 25 surgeons were observed for their surgical technique. Of them, 13(52%) were in group 1: professors 2, associate professors 3, assistant professors 4, senior registrars 4, and 12(48%) were in group 2: senior registrars 7, consultants 2 and specialist medical officers 3 (Table-1).

Of all the patients, 64(48%) came from the two neighbouring districts of Lodhran and Bahawalpur, while the remaining 70(52%) came from Multan,

Table-1: Characteristics of studied cohort.

Sex			
Females		119	88.80 %
Males		15	11.19 %
Age (years)			
Mean		37.17 years	
Standard Deviation		13.41	
Range		14 - 80	
Age Groups			
14 - 20 (years)		16	11.94 %
21 - 40		76	56.71 %
41 - 50		27	20.14 %
51 - 60		11	8.20 %
61 - 70		3	2.23 %
71 - 80		1	0.74 %
Diagnosis			
Euthyroid MNG		105	78.35 %
Toxic MNG		29	21.64 %
Operations			
Total thyroidectomy		95	70.89 %
Near total thyroidectomy		33	24.62 %
Sub-total Thyroidectomy		6	4.47 %
Virtual Groups of Surgeons Observed for Operating Skills			
Group 1		**Group 2**	
Professors	2	Senior registrars	7
Associate professors	3	Consultants	2
Assistant professors	4	Specialist Medical officers	3
Senior registrars	4		

Muzaffargarh, Vehari / Mailsi, Rahim Yar Khan and Bahawalnagar. Total thyroidectomy was performed in 95(70.89%) patients, near-total thyroidectomy in 33(24.62%) and sub-total thyroidectomy in 6(4.47%). For description and analyses, they were bracketed with near-total thyroidectomy cases.

Postoperative transient hypocalcaemia was the most common complication which was found in 15 (11.19%) patients; distributed as: 6 (8.21%) in group 1 and 9 (14.75%) in group 2 (p - 0.23). Permanent hypocalcaemia remained in 1 (1.36%) and 2 (3.27%) in group 1 and group 2 respectively (p - 0.59). Transient dysfunction of RLN resulting in hoarseness of voice, was found in total 9 (6.71%) patients; 3 (4.10%) in group 1 and 6 (9.83%) in group 2. Permanent RLN injury remained in 2 patients and both were in group 2 (p - 0.21). Temporary affection of EBSLN resulting in shallow low pitched voice, was present in total 10 (7.46%) patients: 2 (2.73%) in group 1 and 8 (13.11%) patients in group 2. Permanent injury of EBSLN was recorded in total 3 (2.23%) patients: 1 (1.36%) in group 1 and 2 (3.27%) in group 2 (p - 0.59). There were total five patients who developed postoperative haematoma; one patient in group 1 and 4 in group 2. Thus we see that group 1 patients had fewer complications as compared to group 2, and on certain parameters it was statistically significant (Table-2).

Tracheostomy was performed in 10(7.46%) patients. Of them, 1(0.74%) patient underwent tracheostomy because of tracheomalacia and 5(3.73%) due to longstanding huge MNG in whom postoperative haematoma and respiratory compromise due to tracheal collapse was observed or anticipated. The remaining 4(2.9%) tracheostomies were done in patients who had to be emergently explored on the night following surgery, because of postoperative haematoma and tracheal compression. These patients had toxic MNG. There were 2(1.5%) deaths recorded in the cohort and the responsible factors identified were huge longstanding goitre, old age, haematoma and comorbidities, like heart disease and respiratory tract infection.

Table-2: Complications of thyroid surgery in two groups of cohort of 134 patients.

Complication/event	Total Patients 134		Group 1 (n = 73) 54.47%		Group 2 (n = 61) 45.52%		p-value*
	N	%	N	%	N	%	
Transient Hypocalcaemia	15	11.19	6	8.21	9	14.75	0.23
Permanent Hypocalcaemia	3	2.23	1	1.36	2	3.27	0.59
Transient Recurrent L N palsy	9	6.71	3	4.10	6	9.83	0.30
Permanent RLN palsy	2	1.49%	0	0	2	3.27	0.21
Transient injury of Ext. Br. of sup. L N (EBSLN)	10	7.46	2	2.73	8	13.11	0.04
Permanent injury of Ext. Br. of sup. L N (EBSLN)	3	2.23	1	1.36	2	3.27	0.59
Tracheostomy:							
In Huge long standing	10	7.46	3	4.10	7	11.47	0.18
MNG	5	3.73	3	4.10	2	3.27	1.00
In Toxic MNG	4	2.98	0	0	4	6.55	0.041
In Simple MNG (due to tracheomalacia)	1	0.74	0	0	1	1.63	0.46
Haematoma	5	3.73	1	1.36	4	6.55	0.17

Fischer's exact test for all the variable with < 5 count.

Table-3: Directly Observed Differences in Surgical Technique of two groups of surgeons.

No.	Group 1 Surgeons: Experience >3ys (High volume surgeons)	Group 2 Surgeons: Experience <3ys (Low volume surgeons)
1	Ligation of superior pole vessels individually	En masse ligation of upper pole vessels
2	Capsular dissection and ligation of small branches of inferior thyroid artery individually	Use of artery forceps as markers and di-section of thyroid along these markers.
3	Visual identification of recurrent laryngeal nerve (RLN).	No visual identification of recurrent laryngeal nerve (RLN).
4	Clear identification of parathyroid glands and careful in situ preservation of glands and their blood supply.	Poor identification of parathyroid glands, not preserving the lose tissue along lower pole of thyroid.
5	Meticulous haemostasis: careful ligation of capsular branches of inferior thyroid artery and tracheal branches.	Lack of meticulous haemostatic technique specially at the level of Barry's ligament.
6	Central dissection of capsule	Peripheral dissection of capsule

Discussion

Morbidity is a recognized concern of thyroid surgery. Thyroidectomy-related morbidities are bleeding or haematoma <1%, temporary RLN palsy and hoarseness 3%, permanent hoarseness <1%, temporary hypocalcaemia 5%, permanent hypocalcaemia <1%, seroma, chyle leaks and wound infection 0.05%.[14]

Direct observation of skills through procedure-based assessment (PBA) is now a recognized method for evaluation of OT performance of surgeons. George Miller in his 'pyramid' had identified four levels of assessment for doctors' clinical performance. The top level of performance, 'Does', means doctors' performance in real life[15] The current study developed an observational strategy and noted the differences in surgical technique of different surgeons, and divided them into two virtual groups based on the length of their experience. We compared the rate of complications of thyroid surgery by these two groups of surgeons. This kind of observation-based workplace assessments are now a routine part of training of all grades in all specialties in the United Kingdom.[16] PBA is used in surgical training programmes in the UK to assess surgical skills of trainees in OT.[17]

Present study shows the complications of multinodular goitre surgery in two groups of patients randomly operated by two virtual groups of surgeons differing in their expertise and experience (Table-2). Complications noted in group 1 were relatively fewer and it was obviously due to the superior surgical skills of more experienced surgeons, as directly observed in operating room (Table-3).

Because of vulnerability due to variable anatomic course, the main controversy in thyroid surgery revolves around the issue of recurrent laryngeal nerve preservation by visual identification. RLN palsy is the leading cause of medico-legal litigation for surgeons. RLN injury can occur because of nerve severance, ligation or traction. However it should be less than 1% when thyroidectomy is performed by experienced surgeons, and risk of injury to EBSLN is 20% when upper pole vessels are ligated en masse.[18]

In the current study, permanent RLN palsy in group 1 was none compared to 2(3.27%) in group 2 (p=0.21). When these findings were mapped against the directly-observed surgeons' skills in OT, it was noted that these surgeons were not practising 'capsular dissection', rather they were using artery forceps as 'markers' and were lacking in meticulous technique of haemostasis, especially at the level of Barry's ligament. They were mostly ligating upper pole vessels en masse. These findings indicate an obvious need for improvement in training and technique. Recent results of an audit of patients undergoing total thyroidectomy revealed RLN palsy rate of 1.8% at one month, and 0.5% at 3 months.[19]

Hypocalcaemia which is the most frequent complication after total and near-total thyroidectomy results from inadvertent removal or devascularisation of parathyroid glands during surgery. Postoperative early hypocalcaemia means serum calcium level <8.0mg/dl, measured 24 hours after surgery.[20] Female gender, type of surgical procedure (total thyroidectomy vs. lobectomy), and recurrent goitre are the strong risk factors for hypocalcaemia. In the current study, transient hypocalcaemia was seen in 8.21% in group 1 compared to 14.75% in group 2 (p=0.23). Permanent hypocalcaemia was 1.36% and 3.27% in the two groups, respectively (p=0.59). All of these patients were females. Direct observation revealed that all the surgeons were practicing 'in situ preservation' of parathyroid glands but low rate of hypocalcaemia in group 1 was due to meticulous 'capsular dissection' and preservation of loose tissue at the lower pole of thyroid.[21]

Lahey of Boston (1938) and Riddle from London (1956) advocated routine visual identification of RLN during thyroidectomy. On the other hand the modern technique

and technology of intraoperative nerve-monitoring provides operative information regarding RLN and EBSLN to the surgeon, over and above the direct visualization alone.[21] Various studies have compared visual identification of RLN with intra operative neuro-monitoring, and found no statistically significant difference, except in re-operative and cancer surgeries.[22] IONM has been recommended as a preferred option in patients requiring surgery for thyroid cancer, hyperthyroidism, neck lymph node dissection, second thyroid surgery, retrosternal goiter and/or large thyroid mass with RLN dislocation, transposition of viscera along with suspected non-recurrent RLN.[23] It is also recommended for endoscopic thyroid surgery, repair of RLN injury and parathyroid surgery. As facilities for IONM hardly exist in our high volume thyroid surgery centers, therefore, direct visualization remains the only option to protect the nerves.

Surgeons' experience is one of the most important predictive factors regarding complications of thyroidectomy. William Halstead had stated that "The extirpation of the thyroid gland for goitre typifies better than any operation the supreme triumph of the surgeon's art".[24] Surgeon's annual operative volume has been found to be associated with thyroid surgery outcome. The incidence of complications is much lower in the hands of more experienced or high volume surgeons. And the minimum number of thyroid operations to maintain competence as recommended by a British study is 50 cases/ year.[25] A study sourced from American College of Surgeons revealed 34% less chance of complications from total thyroidectomy if the operating surgeon performs at least 25 cases per year.[26] Some studies have shown that surgeon's performance has a concave association with their length of experience: Increasing surgical case volume and years of practice, is associated with improved performance, and performance may deteriorate toward the end of a surgeon's career.[27]

Direct observation of live thyroid surgeries in operating room revealed that fewer complications in group 1 (Table-3) were due to the better surgical technique: visual identification of recurrent laryngeal nerve, ligating superior thyroid artery branches individually, skillful 'capsular dissection' by ligating tertiary branches of inferior thyroid artery, in situ preservation of parathyroid glands by protecting their blood supply through securing loose tissue at the lower pole of the gland and meticulous technique of haemostasis. While group 2 surgeons were not well versed with 'capsular dissection' but using the conventional technique of applying markers of artery forceps, were ligating superior pole vessels en mass and not consciously preserving the loose tissue along the inferior pole of thyroid.

The obvious differences in the results of surgery by two virtual groups of surgeons have confirmed the significance of 'direct observation' method for workplace based assessment of performance and also proved the relationship of surgeons' experience and technique with the rate of complications. Therefore, direct observation and PBAs can have significant implications for future specialty training and assessment programmes in our country.

On the basis of the findings, the current study recommends that senior surgeons should spare time to directly observe the performance of their junior colleagues in OT and offer feedback to them for continuous improvement in their surgical skills. Also, a serious notice needs to be taken regarding complications of surgery at individual trainee and trainer level, at the unit or ward level in the form of morbidity meetings, and a feedback culture should be adopted at the level of teaching faculty. Finally, post-fellowship training programmes and training modules in different specialties should be encouraged as they can help junior surgeons in improving their surgical skills.

In terms of limitations, the current study could have recorded more data related to patients' histopathological and serological investigation reports.

Conclusion

Surgeons' experience, competence and effectiveness of training are critical factors. Experienced high-volume surgeons, due to their meticulous surgical technique, had better results in thyroid surgery which were reflected in terms of fewer complications in their patients. Besides, direct observation of surgeons' performance in operating room is a significant and top-level indicator in any kind of assessment.

Limitation: Ethical approval from the second activity site could not be accomplished because of hierarchical peculiarities.

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