Original Article

Prediction of the difficult airway by pre-operative ultrasound-based measurement of airway parameters: A prospective observational study

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ABSTRACT

Background and Aims: Ultrasonography has emerged as a new airway assessment tool. However, its role in predicting difficult airways needs to be explored. This study aimed to evaluate the accuracy of pre-operative ultrasound assessment of the neck in predicting difficult airways in patients undergoing elective surgery under general anaesthesia. **Methods:** One hundred and fourteen adult patients undergoing elective surgeries under general anaesthesia were enrolled in this study. In the pre-operative room, upper airway ultrasound measurements of the neck were obtained, namely, distance from skin to the hyoid bone, distance from skin to the thyroid isthmus and thickness of the base of the tongue. Clinical airway assessment details were noted from the pre-anaesthetic evaluation form. The airway management technique was noted. Receiver operating characteristic curves were used to assess the diagnostic value of these upper airway ultrasound measurements in predicting difficult airways. **Results:** The distance from the skin to the thyroid isthmus in the difficult airway group (0.37 ± 0.133 cm) was significantly higher than in the non-difficult group ($P = 0.007$). It appeared to be a better predictor of difficult airways and correlated better with clinical tests among the measured ultrasound parameters. The body mass index was significantly higher in the difficult airway group ($P = 0.009$). **Conclusion:** Considering the difference in means between the two groups, distance from the skin to the thyroid isthmus should be explored as a potential predictor of a difficult airway in studies with a larger sample size.

Key words: Airway, difficult airway, intubation, laryngoscopy, predictors, ultrasonography

INTRODUCTION

Unanticipated difficult airways are potentially life-threatening and remain a significant concern for clinicians managing the airway.[1] The conventional existing clinical parameters for predicting the difficulties associated with airway management remain limited. Ultrasonography is a simple, non-invasive technique used by anaesthesiologists perioperatively.[2,3] Point-of-care ultrasound has also been explored for its beneficial effect on airway management.[4-6] Pre-operative ultrasound measurement of the anterior neck soft-tissue thickness at various levels, in combination with the standard screening tests and assessment tools for difficult laryngoscopy, may enhance the prediction of difficult laryngoscopy.[7,8]

The primary objective of this study was to assess the accuracy of pre-operative ultrasound measurements, namely, distance from skin to the hyoid bone (DSHB), distance from skin to the thyroid isthmus (DSTI) and thickness of the base of the tongue (TBT), with conventional clinical assessment tools to predict difficult airway in patients undergoing elective

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surgery under general anaesthesia. The secondary objective was to correlate the findings of upper airway ultrasound measurements with body mass index (BMI) in predicting difficult airways.

METHODS

This prospective observational study was conducted from June 2022 to March 2023. After approval from the Institutional Human Ethics Committee (vide approval number IHEC-LOP/2022/IL017, dated 23 March 2022), the study was registered in the Clinical Trial Registry - India (vide registration number CTRI/2022/04/042324; https://ctri.nic.in/). Written informed consent was obtained for participation in the study and using patient data from all the study participants for research and educational purposes. The study was carried out according to the principles of the Declaration of Helsinki, 2013.

One hundred fourteen adult patients aged between 18 and 65 years undergoing elective surgeries requiring tracheal intubation under general anaesthesia in various surgical specialities were enrolled. Pregnant patients and patients with head and neck trauma, known facial, cervical, pharyngeal or epiglottic cancer, were excluded from the study. Patients who had undergone previous thyroid surgery, a tracheostomy or were in respiratory distress were also excluded.

All the study participants were kept fasting according to standard guidelines. They were given oral alprazolam 0.25 mg the previous night and on the morning of surgery. Clinical airway assessment details of the modified Mallampati class (MMC) and upper lip bite test (ULBT) were noted from the standard pre-anaesthetic evaluation form.[2] On arrival in the pre-operative room, the upper airway ultrasound measurements were recorded: (a) DSHB with the patient lying supine with head and neck in a neutral position, (b) DSTI with the patient lying supine with head in a neutral position, (c) TBT with the patient lying supine with hyperextension of the neck. All the parameters were noted using a portable ultrasound machine (38 mm broadband [13–6 MHz] linear array transducer [SonoSite Micromaxx SonoSite, Inc., SE Bothwell W.A.]) with the probe placed in the transverse axis.

After wheeling the patients into the operating room, standard monitors were attached. Anaesthesia was induced with intravenous fentanyl (2–3 μg/kg), propofol (1–2 mg/kg) and vecuronium (0.1 mg/kg), and mask ventilation was performed using a face mask. The difficult mask ventilation (DMV) grade was evaluated using the Han scale.[9] After achieving adequate neuromuscular blockade, direct laryngoscopy was attempted for tracheal intubation using an appropriately sized Macintosh blade by an experienced anaesthesiologist (with more than 3 years of experience) blinded to the upper airway ultrasound parameters. The laryngoscopic view was graded according to the Cormack–Lehane (CL) grading and was graded difficult if the CL grade was at least Grade 3, and mask ventilation was graded difficult if the Han scale was at least Grade 3.[10] The presence of at least one of the following was defined as a difficult airway: (a) Han scale Grade 3 or Grade 4 (DMV), (b) CL Grade 3 or Grade 4 (difficult laryngoscopy), (c) MMC Class III or Class IV and (d) ULBT Class III.

The primary outcome measure was to compare the ultrasound parameters (DSHB, DSTI and TBT) between participants with difficult airway and those without difficult airway. The secondary outcome measure was to compare the BMI between participants with difficult airway and those without difficult airway. Receiver operating characteristic (ROC) curves were constructed for all the measured ultrasound parameters (DSHB, DSTI and TBT) against the presence of difficult airway. Optimal cut-off points were estimated using the Youdens index.

The sample size was calculated using the data reported in a previous study, where the mean DSHB in the easy laryngoscopy group was 0.86 cm with a standard deviation (SD) of 0.28 cm, and that of the difficult laryngoscopy group was 1.08 cm with a standard deviation of 0.41 cm.[11] Using G-power software to calculate the mean difference in two independent groups with a type 1 error of 5% and a power of 90%, the estimated sample size was 110. Assuming an attrition rate of around 5%, 115 participants were recruited, and 114 responded. The data were entered in Microsoft Excel version 2013 and analysed using R version 4.2.1. Quantitative data like age, weight, height, BMI and ultrasound parameters were expressed as a mean ± SD, whereas qualitative data like gender and details of clinical assessment tools were represented as numbers and percentages. Receiver Operating Characteristic (ROC) curves were used to assess the diagnostic value of DSHB, DSTI and TBT in predicting difficult airways. The correlation coefficients were calculated for the correlation among

ultrasound parameters. *P* value < 0.05 was considered statistically significant.

RESULTS

The demographic variables, upper airway ultrasound measurements and clinical airway assessment details of DMV and difficult laryngoscopy are summarised in Table 1. In our study population, only one patient had difficulty with mask ventilation (0.9%; Han scale grade DMV4 = 0, DMV3 = 1), and 113 patients had no difficulty with mask ventilation (99.1%; Han scale grade DMV2 = 7, DMV1 = 106). Eight patients had difficult laryngoscopy (7.0%; CL grade CL4 = 0, CL3 = 8), and 106 patients had no difficult laryngoscopy (93.0%; CL grade CL2 = 47, CL1 = 59).

Table 2 shows the demographic, anthropometric and ultrasound parameters distribution between participants with difficult airways and those without. There was no significant difference between the ultrasound parameters of participants with difficult laryngoscopy and those without difficult laryngoscopy by CL grading.

Table 1: Demographic, ultrasound and clinical airway assessment details

Parameter	Values, *n*=114
Age (years)	40.6±13.6
Gender (male/female)	51/63
Weight (kg)	58.6±11.2
Height (cm)	165.0±5.8
BMI (kg/m^2)	21.4±3.4
DSHB (cm)	0.370±0.178
DSTI (cm)	0.331±0.143
TBT (cm)	3.119±0.579
MMC I/II/III/IV	18/59/36/1
ULBT I/II/III	70/37/7
CL grading 1/2/3/4	59/47/8/0
Han scale grading 0/1/2/3/4	0/106/7/1/0

Values are represented as mean±standard deviation or numbers.
BMI - Body mass index; DSHB - Distance from skin to the hyoid bone; DSTI - Distance from skin to thyroid isthmus; TBT - Thickness of the base of the tongue; MMC - Modified Mallampati class; ULBT - Upper lip bite test; CL grading - Cormack–Lehane grading

Table 2: Distribution of demographic, anthropometric and ultrasound parameters between participants with difficult airways and those without

Characteristic	Difficult, *n*=42	Not difficult, *n*=72	*P*
Age (years)	45.1±11.6	38.0±14.0	0.005
Gender (male/female)	15/27	36/36	0.139
Weight (kg)	60.8±10.4	57.3±11.5	0.059
Height (cm)	164.1±5.1	165.6±6.2	0.086
BMI (kg/m^2)	22.5±3.5	20.8±3.3	0.009
DSHB (cm)	0.398±0.191	0.354±0.170	0.212
DSTI (cm)	0.370±0.133	0.308±0.144	0.007
TBT (cm)	3.075±0.540	3.144±0.602	0.681

Values are represented as mean±standard deviation or numbers. BMI - Body mass index; DSHB - Distance from skin to the hyoid bone; DSTI - Distance from skin to thyroid isthmus; TBT - Thickness of the base of the tongue

The area under the ROC curve (AUC) for DSHB was found to be 0.57, while the optimal cut-point was estimated at 0.225 cm, which gave a sensitivity of 97.6% and a specificity of 25%. The AUC for DSTI was found to be 0.65, while the optimal cut-point was estimated at 0.285 cm, which gave a sensitivity of 81% and a specificity of 55.6%. The AUC for TBT was found to be 0.52, while the optimal cut-point was estimated at 3.3 cm, which gave a sensitivity of 73.8% and a specificity of 41.7% [Figure 1]. The sensitivity and specificity table for all the measured ultrasound parameters is available as supplementary file [Supplementary Table 1].The correlation and gender distribution of ultrasound parameters (DSHB, DSTI and TBT) are shown in Figure 2.

DISCUSSION

In this study, we observed that the ultrasound guided DSTI in the difficult airway group was significantly higher than in the non-difficult group. BMI was significantly higher in the difficult airway group. Ultrasound parameters (DSHB, DSTI and TBT) were not statistically significant enough to predict difficult laryngoscopy by CL grading. Similarly, we could not analyse these parameters for DMV as we observed DMV by Han scale grading in only one patient.

Several suprahyoid and infrahyoid ultrasound parameters have been studied with varied results in the literature to predict difficult airways.[12] In a study, the authors showed that distance from the skin to the epiglottis, and the difference of distances from the skin to the epiglottis and skin to glottis had the highest diagnostic accuracy in predicting difficult laryngoscopy.[13] Falcetta *et al*.[14] studied ultrasound measurements of anterior cervical soft tissues at the thyrohyoid membrane and vocal cords. They opined that measurements at the level of the thyrohyoid membrane (pre-epiglottic space) were the best predictors of difficult laryngoscopy. However, they found no correlation between difficult laryngoscopy and measurements at the level of the vocal cords.

In a prospective study, the authors used two ultrasound measurements of the anterior neck at the level of the hyoid bone and the thyrohyoid membrane to predict difficult laryngoscopy. They concluded that both have very strong statistical significance, and DSHB

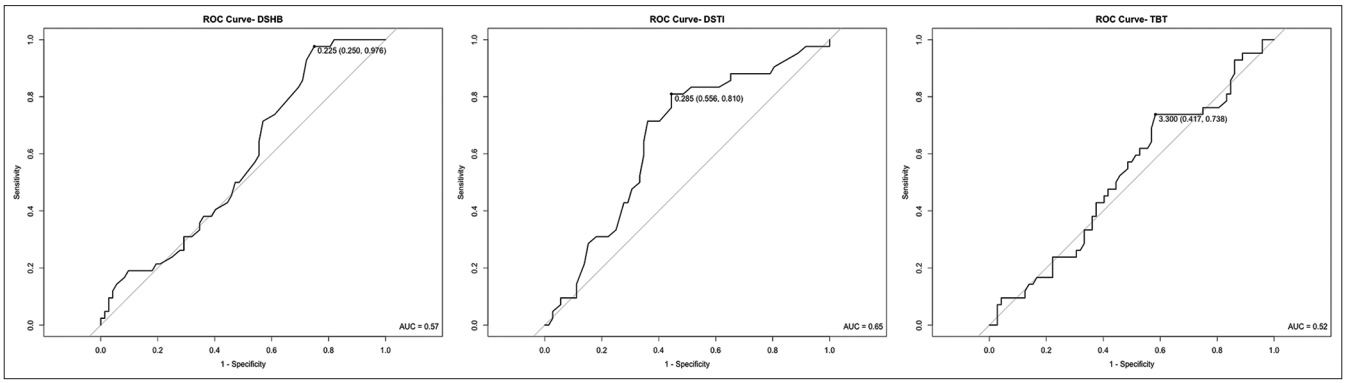

Figure 1: Receiver Operating Characteristic (ROC) curves for ultrasound parameters. DSHB - distance from skin to the hyoid bone; DSTI - distance from skin to thyroid isthmus; TBT- thickness of the base of the tongue

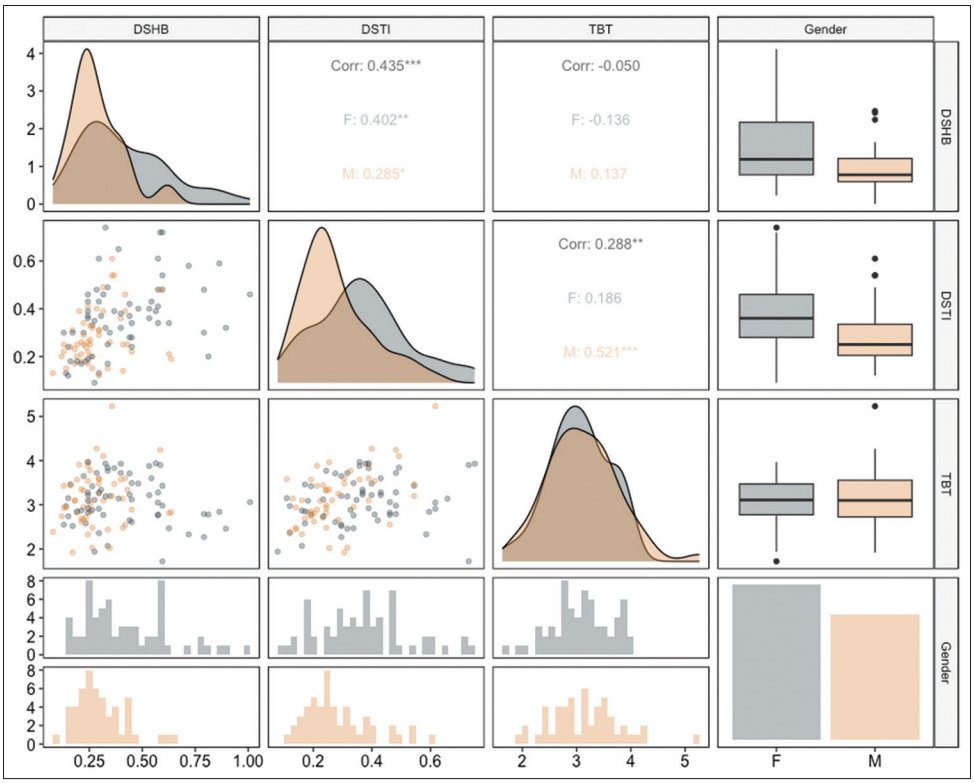

Figure 2: Correlation and gender distribution of measured ultrasound parameters. The panel diagram shows the correlation and distribution of DSHB, DSTI and TBT stratified by gender. The distribution is shown by histograms in the bottom panel (grey for females and orange for males), while density plots are shown in the diagonal cells. The left lower panel shows scatter plots representing the correlation among three variables. It also indicates coloured dots for each gender. The correlation coefficient value is displayed in the right upper quadrant cells where the topmost value is an overall correlation, while others are for correlation among males and females. The right extreme panel shows box plots for DSHB, DSTI and TBT stratified by gender. (DSHB - distance from skin to the hyoid bone; DSTI - distance from skin to thyroid isthmus; TBT- thickness of the base of the tongue; F- female; M- male)

seemed to have a better diagnostic value for predicting a difficult airway in their study.[7] We found similar results; however, we measured distances at the hyoid bone and thyroid isthmus levels. Both were more in the difficult laryngoscopy group, with DSTI being a better predictor of a difficult airway.

Alessandri *et al*.[11] measured five ultrasound measurements of the anterior neck at different levels. Our findings are in accordance with their results. However, we found DSTI to be a better predictor of a difficult airway. In contrast, DSHB was correlated with an increase in the risk for DMV and difficult laryngoscopy in their study. In a recent prospective study, the authors correlated the upper airway ultrasound measurements in the sniffing position. They found that the distance from the skin to the epiglottis was the best predictor of difficult

laryngoscopy.[15] The DSHB was noted to be higher in the difficult laryngoscopy group. Although statistically insignificant, we also found higher DSHB in difficult laryngoscopy and airway groups.

A similar study from Thailand on morbidly obese patients concluded that distance from skin to epiglottis could predict difficult laryngoscopy.[16] In our study, BMI was significantly higher in the difficult airway group [$P = 0.009$; Table 2]. DSTI is a better predictor of difficult airways and is better correlated with clinical assessment tools for difficult airways. Surprisingly, TBT values in our study were lower in difficult laryngoscopy and airway groups than in non-difficult groups [Table 2]. However, they were not statistically significant ($P = 0.681$). This is contrary to the earlier studies, and the reason needs to be clarified.[4,17] These small differences in TBT values might have been caused by slight variations in the pressure the operator applied to the neck while using the ultrasound probe.

DSTI appeared to be a better predictor of difficult airways and correlated better with clinical assessment tools in our study. The measured ultrasound parameters show a significant mean difference between the difficult and non-difficult airway groups and a better AUC for the ROC curve. We found an optimal cut-off value of 0.285 cm for DSTI for predicting difficult airways.

There are certain limitations to our study. First, our study was a single-centre prospective study. Second, our study sample size was small; hence, we had only one DMV case and eight difficult laryngoscopy cases. Our findings were for a population from central India, thus might not apply to other population groups. Third, our results do not apply to patients with distorted airway anatomy or head and neck trauma, as we excluded them from our study. Finally, variations in the sonographer's expertise and the ultrasound machine's properties could have contributed to a certain extent to the disparities in results among different studies. Future multicentric studies with large sample sizes and standardised protocols are required to test the feasibility of anterior neck ultrasound parameters to predict difficult airways and make recommendations.

CONCLUSIONS

We conclude that the measured ultrasound parameters (DSHB, DSTI and TBT) were not statistically significant enough to predict difficult laryngoscopy by CL grading. We could not comment on these parameters for predicting DMV by Han scale grading as we observed DMV in only one patient in our study. However, considering the difference in means between the two groups, distance from the skin to the thyroid isthmus should be explored as a potential predictor of a difficult airway in studies with a large sample size.

Study data availability

De-identified data may be requested with reasonable justification from the authors (email to the corresponding author) and shall be shared after approval as per the authors' Institution policy.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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Supplementary Table 1: Sensitivity & Specificity table for ultrasound parameters

DSHB

Threshold	Sensitivity	Specificity	PPV	NPV	Accuracy
-Inf	100.000000	0.000000	36.84211	NaN	36.84211
0.120	100.000000	1.388889	37.16814	100.00000	37.71930
0.145	100.000000	2.777778	37.50000	100.00000	38.59649
0.155	100.000000	6.944444	38.53211	100.00000	41.22807
0.165	100.000000	9.722222	39.25234	100.00000	42.98246
0.175	100.000000	12.500000	40.00000	100.00000	44.73684
0.185	100.000000	15.277778	40.77670	100.00000	46.49123
0.195	100.000000	18.055556	41.58416	100.00000	48.24561
0.205	97.619048	19.444444	41.41414	93.33333	48.24561
0.215	97.619048	23.611111	42.70833	94.44444	50.87719
0.225	97.619048	25.000000	43.15789	94.73684	51.75439
0.235	92.857143	27.777778	42.85714	86.95652	51.75439
0.245	85.714286	29.166667	41.37931	77.77778	50.00000
0.255	83.333333	30.555556	41.17647	75.86207	50.00000
0.265	73.809524	38.888889	41.33333	71.79487	51.75439
0.275	71.428571	43.055556	42.25352	72.09302	53.50877
0.285	64.285714	44.444444	40.29851	68.08511	51.75439
0.295	59.523810	44.444444	38.46154	65.30612	50.00000
0.305	57.142857	45.833333	38.09524	64.70588	50.00000
0.315	50.000000	51.388889	37.50000	63.79310	50.87719
0.325	50.000000	52.777778	38.18182	64.40678	51.75439
0.335	45.238095	54.166667	36.53846	62.90323	50.87719
0.345	42.857143	55.555556	36.00000	62.50000	50.87719
0.355	40.476190	59.722222	36.95652	63.23529	52.63158
0.365	38.095238	61.111111	36.36364	62.85714	52.63158
0.375	38.095238	63.888889	38.09524	63.88889	54.38596
0.390	35.714286	65.277778	37.50000	63.51351	54.38596
0.405	33.333333	65.277778	35.89744	62.66667	53.50877
0.415	30.952381	68.055556	36.11111	62.82051	54.38596
0.425	30.952381	70.833333	38.23529	63.75000	56.14035
0.435	26.190476	70.833333	34.37500	62.19512	54.38596
0.445	26.190476	72.222222	35.48387	62.65060	55.26316
0.455	23.809524	75.000000	35.71429	62.79070	56.14035
0.475	21.428571	79.166667	37.50000	63.33333	57.89474
0.515	21.428571	80.555556	39.13043	63.73626	58.77193
0.545	19.047619	81.944444	38.09524	63.44086	58.77193
0.560	19.047619	83.333333	40.00000	63.82979	59.64912
0.575	19.047619	84.722222	42.10526	64.21053	60.52632
0.585	19.047619	90.277778	53.33333	65.65657	64.03509
0.595	16.666667	91.666667	53.84615	65.34653	64.03509
0.615	14.285714	94.444444	60.00000	65.38462	64.91228
0.635	11.904762	95.833333	62.50000	65.09434	64.91228
0.680	9.523810	95.833333	57.14286	64.48598	64.03509
0.755	9.523810	97.222222	66.66667	64.81481	64.91228
0.800	4.761905	97.222222	50.00000	63.63636	63.15789
0.835	4.761905	98.611111	66.66667	63.96396	64.03509
0.875	2.380952	98.611111	50.00000	63.39286	63.15789
0.945	2.380952	100.000000	100.00000	63.71681	64.03509
Inf	0.000000	100.000000	NaN	63.15789	63.15789

DSTI

Threshold	Sensitivity	Specificity	PPV	NPV	Accuracy
-Inf	100.000000	0.000000	36.84211	NaN	36.84211
0.105	97.619048	0.000000	36.28319	0.00000	35.96491
0.125	97.619048	2.777778	36.93694	66.66667	37.71930
0.135	97.619048	6.944444	37.96296	83.33333	40.35088

Contd...

Supplementary Table 1: Contd...

DSTI

Threshold	Sensitivity	Specificity	PPV	NPV	Accuracy
0.145	97.619048	8.333333	38.31776	85.71429	41.22807
0.160	95.238095	11.111111	38.46154	80.00000	42.10526
0.175	92.857143	15.277778	39.00000	78.57143	43.85965
0.185	90.476190	19.444444	39.58333	77.77778	45.61404
0.195	88.095238	20.833333	39.36170	75.00000	45.61404
0.205	88.095238	27.777778	41.57303	80.00000	50.00000
0.215	88.095238	30.555556	42.52874	81.48148	51.75439
0.225	88.095238	34.722222	44.04762	83.33333	54.38596
0.235	85.714286	34.722222	43.37349	80.64516	53.50877
0.245	83.333333	38.888889	44.30380	80.00000	55.26316
0.255	83.333333	48.611111	48.61111	83.33333	61.40351
0.265	80.952381	51.388889	49.27536	82.22222	62.28070
0.275	80.952381	52.777778	50.00000	82.60870	63.15789
0.285	80.952381	55.555556	51.51515	83.33333	64.91228
0.295	76.190476	55.555556	50.00000	80.00000	63.15789
0.305	71.428571	59.722222	50.84746	78.18182	64.03509
0.315	71.428571	63.888889	53.57143	79.31034	66.66667
0.325	64.285714	65.277778	51.92308	75.80645	64.91228
0.335	59.523810	65.277778	50.00000	73.43750	63.15789
0.345	52.380952	66.666667	47.82609	70.58824	61.40351
0.355	50.000000	66.666667	46.66667	69.56522	60.52632
0.365	47.619048	69.444444	47.61905	69.44444	61.40351
0.375	42.857143	70.833333	46.15385	68.00000	60.52632
0.385	42.857143	72.222222	47.36842	68.42105	61.40351
0.395	33.333333	75.000000	43.75000	65.85366	59.64912
0.405	30.952381	77.777778	44.82759	65.88235	60.52632
0.415	30.952381	80.555556	48.14815	66.66667	62.28070
0.425	30.952381	81.944444	50.00000	67.04545	63.15789
0.445	28.571429	84.722222	52.17391	67.03297	64.03509
0.470	21.428571	86.111111	47.36842	65.26316	62.28070
0.485	14.285714	88.888889	42.85714	64.00000	61.40351
0.515	9.523810	88.888889	33.33333	62.74510	59.64912
0.560	9.523810	93.055556	44.44444	63.80952	62.28070
0.585	9.523810	94.444444	50.00000	64.15094	63.15789
0.600	7.142857	94.444444	42.85714	63.55140	62.28070
0.630	4.761905	97.222222	50.00000	63.63636	63.15789
0.685	2.380952	97.222222	33.33333	63.06306	62.28070
0.730	0.000000	98.611111	0.00000	62.83186	62.28070
Inf	0.000000	100.000000	NaN	63.15789	63.15789

TBT

Threshold	Sensitivity	Specificity	PPV	NPV	Accuracy
Inf	100.000000	0.000000	36.84211	NaN	36.84211
4.750	100.000000	1.388889	37.16814	100.00000	37.71930
4.255	100.000000	2.777778	37.50000	100.00000	38.59649
4.170	100.000000	4.166667	37.83784	100.00000	39.47368
4.035	97.619048	4.166667	37.27273	75.00000	38.59649
3.965	95.238095	4.166667	36.69725	60.00000	37.71930
3.950	95.238095	5.555556	37.03704	66.66667	38.59649
3.935	95.238095	6.944444	37.38318	71.42857	39.47368
3.920	95.238095	9.722222	38.09524	77.77778	41.22807
3.905	95.238095	11.111111	38.46154	80.00000	42.10526
3.890	92.857143	11.111111	37.86408	72.72727	41.22807
3.860	92.857143	13.888889	38.61386	76.92308	42.98246
3.835	90.476190	13.888889	38.00000	71.42857	42.10526
3.800	88.095238	13.888889	37.37374	66.66667	41.22807

Contd...

Supplementary Table 1: Contd...

TBT

Threshold	Sensitivity	Specificity	PPV	NPV	Accuracy
3.745	85.714286	15.277778	37.11340	64.70588	41.22807
3.715	80.952381	15.277778	35.78947	57.89474	39.47368
3.680	80.952381	16.666667	36.17021	60.00000	40.35088
3.625	78.571429	16.666667	35.48387	57.14286	39.47368
3.590	76.190476	19.444444	35.55556	58.33333	40.35088
3.575	76.190476	20.833333	35.95506	60.00000	41.22807
3.555	76.190476	23.611111	36.78161	62.96296	42.98246
3.515	76.190476	25.000000	37.20930	64.28571	43.85965
3.485	73.809524	25.000000	36.47059	62.06897	42.98246
3.475	73.809524	27.777778	37.34940	64.51613	44.73684
3.465	73.809524	29.166667	37.80488	65.62500	45.61404
3.450	73.809524	30.555556	38.27160	66.66667	46.49123
3.435	73.809524	31.944444	38.75000	67.64706	47.36842
3.425	73.809524	34.722222	39.74359	69.44444	49.12281
3.385	73.809524	36.111111	40.25974	70.27027	50.00000
3.345	73.809524	37.500000	40.78947	71.05263	50.87719
3.330	73.809524	40.277778	41.89189	72.50000	52.63158
3.300	73.809524	41.666667	42.46575	73.17073	53.50877
3.265	69.047619	43.055556	41.42857	70.45455	52.63158
3.240	66.666667	43.055556	40.57971	68.88889	51.75439
3.225	64.285714	43.055556	39.70588	67.39130	50.87719
3.210	61.904762	44.444444	39.39394	66.66667	50.87719
3.195	61.904762	47.222222	40.62500	68.00000	52.63158
3.170	59.523810	47.222222	39.68254	66.66667	51.75439
3.145	59.523810	48.611111	40.32258	67.30769	52.63158
3.130	57.142857	50.000000	40.00000	66.66667	52.63158
3.115	57.142857	51.388889	40.67797	67.27273	53.50877
3.105	54.761905	51.388889	39.65517	66.07143	52.63158
3.095	52.380952	54.166667	40.00000	66.10169	53.50877
3.075	50.000000	55.555556	39.62264	65.57377	53.50877
3.055	47.619048	55.555556	38.46154	64.51613	52.63158
3.020	47.619048	56.944444	39.21569	65.07937	53.50877
2.985	47.619048	58.333333	40.00000	65.62500	54.38596
2.975	45.238095	58.333333	38.77551	64.61538	53.50877
2.960	45.238095	59.722222	39.58333	65.15152	54.38596
2.945	42.857143	59.722222	38.29787	64.17910	53.50877
2.935	42.857143	61.111111	39.13043	64.70588	54.38596
2.925	42.857143	62.500000	40.00000	65.21739	55.26316
2.915	40.476190	62.500000	38.63636	64.28571	54.38596
2.900	38.095238	62.500000	37.20930	63.38028	53.50877
2.885	38.095238	63.888889	38.09524	63.88889	54.38596
2.875	35.714286	63.888889	36.58537	63.01370	53.50877
2.860	33.333333	63.888889	35.00000	62.16216	52.63158
2.845	33.333333	66.666667	36.84211	63.15789	54.38596
2.835	30.952381	66.666667	35.13514	62.33766	53.50877
2.825	28.571429	66.666667	33.33333	61.53846	52.63158
2.815	26.190476	68.055556	32.35294	61.25000	52.63158
2.800	26.190476	69.444444	33.33333	61.72840	53.50877
2.785	23.809524	69.444444	31.25000	60.97561	52.63158
2.775	23.809524	72.222222	33.33333	61.90476	54.38596
2.765	23.809524	73.611111	34.48276	62.35294	55.26316
2.750	23.809524	75.000000	35.71429	62.79070	56.14035
2.725	23.809524	77.777778	38.46154	63.63636	57.89474
2.700	21.428571	77.777778	36.00000	62.92135	57.01754
2.675	19.047619	77.777778	33.33333	62.22222	56.14035

Contd...

Supplementary Table 1: Contd...					
TBT					
Threshold	**Sensitivity**	**Specificity**	**PPV**	**NPV**	**Accuracy**
2.655	16.666667	77.777778	30.43478	61.53846	55.26316
2.635	16.666667	79.166667	31.81818	61.95652	56.14035
2.615	16.666667	80.555556	33.33333	62.36559	57.01754
2.595	16.666667	81.944444	35.00000	62.76596	57.89474
2.565	16.666667	83.333333	36.84211	63.15789	58.77193
2.535	14.285714	84.722222	35.29412	62.88660	58.77193
2.500	14.285714	86.111111	37.50000	63.26531	59.64912
2.475	11.904762	87.500000	35.71429	63.00000	59.64912
2.465	9.523810	87.500000	30.76923	62.37624	58.77193
2.450	9.523810	88.888889	33.33333	62.74510	59.64912
2.415	9.523810	90.277778	36.36364	63.10680	60.52632
2.375	9.523810	91.666667	40.00000	63.46154	61.40351
2.345	9.523810	93.055556	44.44444	63.80952	62.28070
2.300	9.523810	95.833333	57.14286	64.48598	64.03509
2.170	7.142857	95.833333	50.00000	63.88889	63.15789
2.050	7.142857	97.222222	60.00000	64.22018	64.03509
2.025	4.761905	97.222222	50.00000	63.63636	63.15789
1.980	2.380952	97.222222	33.33333	63.06306	62.28070
1.930	0.000000	97.222222	0.00000	62.50000	61.40351
1.820	0.000000	98.611111	0.00000	62.83186	62.28070
-Inf	0.000000	100.000000	NaN	63.15789	63.15789