Impact of early versus late tracheotomy on diaphragmatic function assessed by ultrasonography in mechanically ventilated stroke patients

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ABSTRACT

Background: Cerebrovascular stroke is one of the most disabling chronic conditions, as it is often associated with devastating long-term neurologic deficits. Design: A prospective observational study. Setting: Critical Care Units of Alexandria Main University Hospital. Patients: 60 adult mechanically ventilated stroke patients of both genders according to sample size calculation. Objective: Compare the outcome of early versus late tracheotomy on diaphragmatic function, assessed by ultrasonographic assessment in mechanically ventilated stroke patients. Methods: Patients were randomized blindly into two groups: group I was subjected to early bedside percutaneous tracheotomy within 4 days of ICU stay, while group II was tracheostomized after 14 days. A Sonosite Mindray DP10 2015–08 with a 3–5 MHz linear probe was used to assess the diaphragm daily before and after tracheotomy. Measures taken were diaphragmatic excursion (DE) and diaphragmatic thickness (DT). Primary outcome was impact of early tracheotomy on diaphragmatic ultrasound measurements. Secondary outcomes were mechanical ventilation, ICU stay, and 28-day mortality. Results: After tracheotomy, a significant improvement in DE and DTF in group I was encountered more than group II (p < 0.01). There was a significant decrease in ventilator days, and ICU stay in group I (p < 0.01), without statistical significance in the 28-day mortality (p = 0.612). Conclusion: Early tracheotomy in mechanically ventilated stroke patients could improve diaphragmatic ultrasound measurements resulting in rapid weaning off mechanical ventilation and less ICU stay without significant effect on 28-day mortality.

1. Introduction

Stroke is the second cause of death worldwide. In the United States, it is the fifth cause of death with nearly 800,000 Americans experiencing recent stroke annually [1]. In Egypt, prevalence of stroke is high with a crude prevalence rate of 963/100,000 inhabitants. It accounts for 6.4% of all deaths and is considered as the third cause of death in Egypt [2]. Patients may have impaired bulb function due to the stroke injury itself. To maintain patent airway and avoid aspiration, they may need temporary intubation and in sequence mechanical ventilation despite having preserved consciousness [3].

As long as airway protection is just temporary by endotracheal intubation, weaning off stroke patients will be a challenging process and so it will never be easy except after a more definitive airway like tracheotomy that can facilitate weaning with secured airways. The stroke-related early tracheotomy (SET) score was used in the SETPOINT trial as an early screening tool for anticipating prolonged intubation in cerebrovascular stroke patients with a score of more than 8 defining the need for early tracheotomy [4,5].

Prolonged ventilation in these patients leads to diaphragmatic dysfunction (DD) that can occur early or late in course of mechanical ventilation because of critical care weakness, a phenomenon which is called ventilator-induced DD [6]. Tracheotomy in stroke patients provides a definitive securing to compromised airways, making such patients ready for weaning off mechanical ventilation. Early tracheotomy may decrease incidence of pneumonia, duration of mechanical ventilation, ICU stay, and mortality in these patients [4–6].

Ultrasoundography is a feasible bedside tool to assess diaphragm function and morphology by allowing quantification of thickness and contractility. This can successfully predict respiratory function and successful weaning from mechanical ventilation [7–9]. There are two common diaphragm sonographic measures: the diaphragmatic excursion (DE) and the diaphragmatic thickness (DT) fraction (DTF) [10–12]. Aim of this work was to assess the impact of early tracheotomy on diaphragmatic function, assessed by ultrasonographic assessment, in mechanically ventilated stroke patients. Primary outcome was impact of early tracheotomy on...
diaphragmatic ultrasound measurements. Secondary outcomes were impact on days of mechanical ventilation, ICU stay, and 28-day mortality.

2. Patients and methods

This prospective observational study was carried out on 60 adult patients of both genders according to sample size calculation. Thirty patients with successful weaning and another 30 patients who failed weaning from mechanical ventilation produced an 80% power to detect an AUC of 0.79 for using ultrasound as a predictive tool for diaphragm function in mechanically ventilated stroke patients and its impact on weaning off mechanical ventilation, using ROC curve analysis with a significance level (alpha) of 0.05 [13,14]. Sample size was calculated using MedCalc statistical software.

Patients were admitted to Critical Care Medicine Department in Alexandria Main University Hospital. Approval of the Medical Ethics Committee of Alexandria Faculty of Medicine was obtained. An informed consent was taken from the patients’ next of kin before their enrollment in the study.

Inclusion criteria were adult ischemic stroke patients who required intubation and mechanical ventilation for airway protection due to bulbar dysfunction with an SET score of more than 8, anticipating the need for prolonged intubation. Exclusion criteria were pregnant females, those who refused early tracheotomy, patients presented with neck distortion due to trauma or tumors, patients with previous diaphragmatic weakness or paralysis, and those with difficult ultrasonographic view or assessment, e.g., pneumothorax, surgical emphysema, or chest deformities.

All patients upon intubation were consecutively ventilated using synchronized intermittent mandatory ventilation mode. Ventilator was set to deliver tidal volume 6–8 ml/kg, respiratory rate 10–16/minute to allow for spontaneous breathing, positive end-expiratory pressure 5 cmH2O, and pressure support (PS) 15 cmH2O. They were subjected on admission to collection of demographic data (age and sex), patients’ comorbidities, site of stroke (according to brain CT findings), indication for intubation, and SET score (Table 1). The SET score was used as a screening tool for anticipating prolonged intubation in stroke patients with a score of more than 8. Dysphagia was assessed by a non-successful swallowing test, impaired saliva handling, or loss/reduction of gag reflex. For each physiological variable, the worst value in the first 24 hours after admission was used to achieve an estimation as early as possible [4,5].

According to timing of tracheotomy, enrolled patients were randomly (even odd randomization) assigned into two groups: group I was subjected to early bedside percutaneous tracheotomy using Griggs’ dilating forceps technique within 4 days of intubation and ventilation, while group II was tracheotomized after 14 days [15–17].

A Sonosite Mindray DP10 2015–08 (China) with a 3–5 MHz linear probe was used to assess the diaphragm at the zone of apposition, between the 8th and 10th intercostal space in the mid-axillary or anterior axillary line, 0.5–2 cm below the costophrenic sinus. At a depth of 1.5–3 cm, two parallel echogenic layers could be identified: the nearest line was the parietal pleura and the deeper one was the peritoneum. The diaphragm is the less echogenic structure in between these two lines (Figure 1a). This approach was utilized to assess DT and thickening with inspiration, in B- & M-mode (Figure 1b). In healthy, spontaneously breathing subjects, the normal thickness of the diaphragm at the zone of apposition is 1.7 ± 0.2 mm while relaxing, increasing to 4.5 ± 0.9 mm on deep inspiration [18]. End-expiratory DT was measured in three consecutive respiratory cycles during the end-expiratory pause and measurements were averaged. DTF was calculated using the formula: (end-inspiratory DT – end-expiratory DT)/end-expiratory DT × 100 [9–12].

In the subcostal area, between the mid-clavicular and anterior axillary lines, using liver or spleen as acoustic windows, diaphragm was identified as a hyperechoic line (produced by the pleura tightly adherent to the muscle) that approaches the probe during inspiration (Figure 1c). The inspiratory excursion (DE) was measured in M-mode (Figure 1d). In healthy subjects during quiet spontaneous breathing, diaphragm inspiratory excursion was found to be 13.4 ± 0.18 mm [8,18]. Both DE and DTF were measured and calculated once daily till performing early or late tracheotomy in both groups I & II consecutively and continued until weaning off mechanical ventilation. DD was diagnosed by DE less than 15 mm and DTF less than 20% [12].

All enrolled patients were managed and followed up according to local policies and guidelines for managing mechanically ventilated stroke patients all

| Table 1. SET score [4,5]. |
|---------------------------|
| Area of assessment        | Situation       | Points |
| Neurological function     | Dysphagia       | 4      |
|                          | Observed aspiration | 3     |
|                          | GCS on admission < 10 | 3    |
| Neurological lesion       | Brain stem      | 4      |
|                          | Space occupying lesion | 3     |
|                          | Ischemic infarct > 2/3 MCA territory | 4     |
|                          | ICH > 25 ml      | 4      |
|                          | Diffuse lesion   | 3      |
|                          | Hydrocephalus    | 4      |
| Extra-cerebral organ      | Neurological intervention | 2     |
| Function/procedure        | Additional respiratory disease | 3     |
|                          | PaO2/FiO2 < 150  | 2      |
|                          | APACHE II > 20   | 4      |
|                          | Lung Injury Score > 1 | 2     |
|                          | Sepsis          | 3      |
through their ICU stay. Primary outcome was impact of early tracheotomy on diaphragmatic ultrasound measurements (DE and DTF). Secondary outcomes were impact on days of mechanical ventilation, ICU stay, and 28-day mortality.

**Statistical analysis:** Data were fed to the computer using IBM SPSS software package version 24.0. Qualitative data were described using number and percent. Comparison between different groups regarding categorical variables was tested using Chi-square test. Quantitative data were described using mean and standard deviation for normally distributed data. For normally distributed data, comparison between two independent population was done using independent t-test, while if more than two population were analyzed F-test (ANOVA) was used. Significance test results were quoted as two-tailed probabilities. Significance of the obtained results was judged at the 5% level.

3. Results

**Figure 1.** DT at zone of apposition in a: B-mode, b: M-mode. 1 Thickness at end-expiration, 2 thickness at end-inspiration. DE, right subcostal in c B-mode, d M-mode.

**Figure 2.** Patients’ flow chart.
Table 2. Baseline patient’s criteria in both studied groups at time of enrollment.

|                      | Group I       | Group II      | χ²  | p       |
|----------------------|---------------|---------------|-----|---------|
| Age (years)          | 28–68         | 22–72         | 1.415 | 0.549  |
| Range                | 61.3 ± 22.6   | 58.6 ± 20.3   |     |         |
| Mean ± S.D.          |               |               |     |         |
| Sex                  | 21 (70%)      | 18 (60%)      | 1.03 | 0.612  |
| Male                 | 9 (30%)       | 12 (40%)      |     |         |
| Female               |               |               |     |         |
| Comorbidities        |               |               |     |         |
| Diabetes Mellitus    | 28 (93.3%)    | 27 (90%)      | 2.218 | 1.000  |
| Hypertension         | 16 (53.3%)    | 18 (60%)      | 0.271 | 0.602  |
| Cardiac              | 9 (30%)       | 7 (23.3%)     | 0.341 | 0.599  |
| Renal                |               |               |     |         |
| Stroke site          | 7 (23.3%)     | 9 (30.0%)     | 4.106 | 0.250  |
| Brain stem           | 7 (23.3%)     | 7 (23.3%)     |     |         |
| Right side           | 10 (33.3%)    | 13 (43.3%)    |     |         |
| Left side            | 6 (20.0%)     | 1 (3.3%)      |     |         |
| Occipital            |               |               |     |         |
| Indication of intubation | 12 (40.0%)  | 16 (53.3%)    | 1.071 | 0.301  |
| GCS <8               | 18 (60.0%)    | 14 (46.7%)    |     |         |
| Bulbar manifestation |               |               |     |         |
| SET score            | 8 (26.7%)     | 5 (16.7%)     | 1.316 | 0.518  |
| 8–10                 | 12 (40.0%)    | 16 (53.3%)    |     |         |
| 11 – 13              | 10 (33.3%)    | 9 (30.0%)     |     |         |
| ≥14                  |               |               |     |         |

Values are presented as mean ± standard deviation (SD), number (n), and percentage (%). SET score: stroke-related early tracheotomy score. χ²: Chi-square test. p: probability for comparing between both groups. *: significant differences from baseline p ≤ 0.05.

Figure 2. Patients’ flow chart. Current study was carried out on 60 adult mechanically ventilated stroke patients of both sexes. They were assigned into two groups using simple randomization (even odd randomization method). Group I included 30 patients who were subjected to early percutaneous dilational tracheotomy. Group II included 30 patients who were subjected to percutaneous dilational tracheotomy after 14 days.

Table 1 shows the components of SET Score. Table 2 shows that there was no statistically significant difference between the two studied groups regarding age, sex, and comorbidities (p > 0.05). It showed also that there was no significant difference between the two groups regarding stroke site, indications of intubation, and SET score (p > 0.05).

Table 3 shows that there was no significant difference between both groups in diaphragmatic measurements before performing tracheotomy. After performing tracheotomy, there was a highly significant increase in DE and DTF in the early group I more than the late group II (p < 0.01).

Table 4 shows that there was a highly significant decrease in ventilator days, and ICU stay in group I more than group II (p < 0.01), without statistical significance in the 28-day mortality between both groups (p = 0.612).

Table 5 shows that overall ventilator days and ICU stay for all patients showed significantly negative correlation with both DE and DTF.

4. Discussion

Baseline patients’ criteria like age, sex, comorbidities, stroke site, indications of intubation, and SET score were homogenous without statistical significance in both studied groups, trying to make timing of tracheotomy in such mechanically ventilated stroke patients the main variable all through the study.

According to the present study, there was no significant difference between both groups in diaphragmatic measurements before performing tracheotomy. After performing tracheotomy, a highly significant improvement in DE and DTF in the early group I was encountered more than the late group II (p < 0.01). Such findings can be explained that performing tracheotomy as a definitive airway in this group of patients made them more liberal in spontaneous breathing during ventilation without additional risk of aspiration if their endotracheal tubes were removed without securing their airways and so were more eligible for weaning off mechanical ventilation that was only applied to them because of compromised airways. In other words, for intubated stroke patients in our study, timing of tracheotomy could decide readiness for weaning off MV, and when tracheotomy had been done earlier, less DD had been encountered rendering weaning process easier.

In agreement with our study, Ali et al. [12] studied the diaphragmatic ultrasound measurements as possible predictors of weaning outcome in mechanically ventilated patients due to diverse pathologies. The mean DE in short period MV was 20 mm and in prolonged MV was 15 mm, and DTF in short period MV was 45.0% and in prolonged MV was 37.0%, and this was statistically significant. They found that DD is more encountered with prolonged MV.

Table 3. Diaphragmatic ultrasound measurements in both studied groups.

|                      | Before Tracheotomy |               | After Tracheotomy |               | t-test |
|----------------------|--------------------|---------------|-------------------|---------------|--------|
|                      | Group I            | Group II      | t-test            | Group I       | Group II | t-test |
| DE (mm):             | 11–18              | 11–17         | 0.12              | 12.0–19.0     | 8.0–13.0 | 4.98   |
| Range                | 15.0 ± 2.1         | 14.0 ± 2.12   | p: 0.71           | 16.23 ± 1.74  | 9.87 ± 1.63 | p: 0.001* |
| Mean ± S.D.          |                    |               |                   |               |         |
| DTF (%):             | 45–55              | 44–54         | 0.22              | 42.0–79.0     | 20.0–40.0 | 4.77   |
| Range                | 49.3 ± 3.25        | 49.1 ± 3.24   | p: 0.62           | 59.03 ± 11.55 | 28.97 ± 6.47 | p: 0.001* |
| Mean ± S.D.          |                    |               |                   |               |         |

Values are presented as mean ± standard deviation (SD), and range. DE: diaphragmatic excursion. DTF (%): diaphragmatic thickness fraction. Percentage. t: student t-test. p: probability for comparing between both groups. *: significant differences from baseline p ≤ 0.05.
Table 4. Secondary outcome in both studied groups.

| Ventilator days | Group I | Group II | t-test | p-value |
|-----------------|---------|----------|--------|---------|
| Range           | 1.0–38.0| 9.0–39.0 | 6.25   | 0.001*  |
| Mean ± S.D.     | 10.83 ± 8.75 | 23.77 ± 8.80 | 5.21 | 0.001* |
| ICU stay (days) | 4.0–30.0 | 12.0–40.0 |        |         |
| Mean ± S.D.     | 11.93 ± 7.14 | 24.97 ± 8.97 |        |         |
| 28-day mortality| 1 (3.3%) | 3 (10%)  | 1.071  | 0.612   |

Values are presented as mean ± standard deviation (SD), and range. t: student t-test; p: probability for comparing between both groups. *: significant differences from baseline p ≤ 0.05.

Table 5. Correlation of diaphragmatic ultrasound measurements to overall ventilator days & ICU stay in all studied patients

| Ventilator days | ICU stay |
|-----------------|----------|
| DE Pearson Correlation | −0.625* | −0.619* |
| Significance (2-tailed) | 0.0001 | 0.0001 |
| DTF Pearson Correlation | −0.902* | −0.474* |
| Significance (2-tailed) | 0.0001 | 0.0001 |

DE: diaphragmatic excursion. DTF: diaphragmatic thickness fraction. *: significant differences from baseline p ≤ 0.05.

Petrof et al. [19] also concluded in their study that DD is a common complication in mechanically ventilated patients and is a reasonable cause of weaning failure. Dinino et al. [14] explored DT measurement by ultrasound rather than the diaphragm motion to predict extubation outcome in any patient ventilated due to respiratory failure regardless of the etiology. They concluded that this method may be of benefit in reducing the number of failed extubations.

Present study showed that there was a highly significant decrease in ventilator days, and ICU stay in group I more than group II (p < 0.01), without statistical significance in the 28-day mortality between both groups (p = 0.612). To assess the value of diaphragmatic ultrasound in predicting successful weaning, Kim et al. [11] concluded in their study that DD was diagnosed by ultrasound if an excursion <10 mm or a paradoxical movement was observed. DD was associated with weaning failure, and so, ultrasound may recognize patients at risk of difficult and failed weaning.

Hermans et al. [7] showed that patients with DD had a markedly worse prognosis when diaphragmatic force was measured by transdiaphragmatic pressure measurements during bilateral magnetic stimulation of the phrenic nerves. They concluded that successful weaning was found among 28/60 of the included mechanically ventilated patients (2 with DD and 26 without DD), and the total number of patients with weaning failure (primary and secondary) with and without DD was 26/60 (21 with DD and 5 without DD).

In contrast to our results, Umbrello et al. [20] concluded that in 25 postoperative patients on assisted spontaneous breathing, DT was a good indicator of changes of inspiratory muscle effort in response to modifications of PS level while using DE as an indicator was of little help during PSV. However, they recommended to assess if this holds true in a greater number of patients with different pathologies.

In our study, the results showed that the ventilation days and ICU stay were significantly lower in the early group than in the late group, while the mortality rate was insignificant between both groups. Shaw et al. [21] compared early tracheotomy (<7 days) and late tracheotomy (>10 days) in ICU. A total of 49,191 patients from 185 different medical centers were analyzed. The survival rates were higher in patients who had early tracheotomy. Incidence of VAP, ICU stay, in-hospital stay, and mortality was lower in patients who had an early tracheotomy (P < 0.0001).

Devarajan et al. [22] reported in their 114-patient study that early tracheotomy (<10 days) was associated with lower mortality (21.1% vs 40.4%) and morbidity (14 vs 33%) rather than late tracheotomy (>14 to 28 days). Besides that, infection rates, tracheal aspiration, and positive blood culture rates were statistically lower in the early tracheotomy.

In contrast to our study, Young et al. [23] conducted a randomized study that investigated early versus late tracheotomy (The TracMan study). In this multicenter trial, patients from over 70 ICUs with different pathologies were randomized to early (within 4 days) or late tracheotomy (after 10 days) groups. No difference was noted in ventilation days, ICU days, and early and late mortality between groups. They concluded that early tracheotomy does not improve significant clinical outcomes. This discrepancy may be explained that in our study we chose only stroke patients who were intubated and ventilated mostly to secure their airways making them eligible for weaning immediately after being tracheostomized.

Our outcome data were similar to the results of a meta-analysis by McCredie and colleagues [24], looking at early tracheotomy in patients with severe acute brain injury. They found that although early tracheotomy reduced length of ICU stay, it did not reduce mortality. Despite lack of direct evidence, they still believe that early tracheotomy likely reduces total ventilator time eliminating the primary risk factor for VAP, which is the ventilator itself.

Ventilator days and ICU stay in the present study showed significantly negative correlation with both DE and DTF. In agreement with our study, Zhang et al. [25] studied the diaphragm ultrasound as a predictive tool for extubation outcome. In this study, they found that the diaphragm ultrasound parameters were significantly higher in the success more than failure group of patients. Li et al. [26] studied diaphragmatic ultrasonography for predicting success of ventilator weaning. In this meta-analysis, the pooled sensitivities for DE and DTF were 0.786 and 0.893, and the pooled specificities were 0.711 and 0.796, respectively.
Coiffard et al. [27] studied the diaphragm echodensity in mechanically ventilated patients. They found that changes in DT over time were associated with increases in echodensity, such increase was associated with prolonged mechanical ventilation. They noted that changes in diaphragm echodensity appeared mostly by day 2 after ICU admission, highlighting a rapid process most likely related to the primary cause of the acute respiratory failure or possibly resulting from injurious respiratory effort during mechanical ventilation.

This study had some limitations. First is the small number of patients despite appropriateness to calculated sample size. Another point is that some patients were not fit for early tracheotomy due to emerging clinical problems not addressed in the study as exclusion criteria like shock state or bleeding tendency, in such cases tracheotomy was delayed, and this may misinterpret secondary outcomes in relation to timing of tracheotomy.

5. Conclusion

Early tracheotomy in mechanically ventilated stroke patients could improve diaphragmatic ultrasound measurements, namely DE and DTF, resulting in rapid weaning off mechanical ventilation and less ICU stay without significant effect on 28-day mortality.

Disclosure statement

No potential conflict of interest was reported by the author(s).

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