

The Feasibility of Domiciliary Non-Invasive Mechanical Ventilation due to Chronic Respiratory Failure in Very Elderly Patients

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Abstract

OBJECTIVES: The aim of this study was to investigate the use of domiciliary non-invasive mechanical ventilation (NIMV) in very elderly patients (age 80 and over).

MATERIALS AND METHODS: This retrospective study included a total of 44 patients aged 80 years or older, who were admitted to the Health Sciences University, Süreyyapaşa Chest Diseases and Thoracic Surgery Training and Research Hospital, Pulmonary Intensive Care Outpatient Clinic between 2012 and 2018 and applied NIMV for chronic respiratory failure. The patients were divided into two groups: survivors (n=15) and non-survivors (n=29). Data were obtained from the retrospectively formed hospital database. The characteristics of patients, comorbidities, NIMV compliance, pulmonary function tests, and blood gas analyses were compared between the survivors and non-survivors.

RESULTS: From the retrospective analysis of 44 cases, the non-survivors were found to have a significantly shorter duration of domiciliary NIMV (737 days vs. 890 days, $p=0.027$) and lower hemoglobin concentration (11.1 g/L vs. 12.9 g/L, $p=0.004$). The number of comorbid conditions, pulmonary function test, and blood gas analyses results did not differ significantly between the groups. Compliance was moderate in this elderly population, at 4.9 ± 1.9 h/day (range: 0.8-9.1 h/day). NIMV was well-tolerated in 36 of the 44 elderly patients (81.8%). Overall mortality was 65.9%.

CONCLUSION: Domiciliary NIMV can be of benefit to very elderly patients, and age is not an obstacle. Therefore, this population should not be excluded from this treatment solely on the basis of age.

KEYWORDS: Clinical problems, COPD, health policies, pulmonary rehabilitation and chronic care, respiratory intensive care

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INTRODUCTION

In the treatment of chronic respiratory failure (CRF), home mechanical ventilation (HMV) is a mode of ventilatory support applied in patient's home. The use of HMV has become increasingly widespread over the last two decades [1]. HMV is defined as intermittent or continuous use of an HMV device at home, using an integral (non-invasive) or a tracheostomy tube (invasive) [2]. Domiciliary non-invasive mechanical ventilation (NIMV) is primarily used in the treatment of chronic obstructive pulmonary disease (COPD), obesity hypoventilation syndrome (OHS), neuromuscular diseases, and restrictive chest wall disorders [3]. In a previous study from Turkey, the main estimated indications were listed as COPD (75%), OHS (10%), overlap syndrome (10%), and restrictive lung disorders (5%) [4].

In previous studies examining domiciliary NIMV application, beneficial effects have been reported, such as an improvement in hypercapnia and hypoxemia, increased respiratory functions and the efficacy of pulmonary rehabilitation, increased quality of life (QoL) because of improved sleep quality, and reduced hospital admissions, intensive care admissions, the frequency of intubations, and costs [4-6]. There are few studies comparing whether the HMV treatment prolongs life expectancy [4-7]. According to the results of those studies, life expectancy was increased in neuromuscular diseases (poliomyelitis sequelae, spinal muscular atrophy, muscular dystrophy, myotonic dystrophy, amyotrophic lateral sclerosis), the presence of thoracic kyphoscoliosis, and tuberculosis sequelae, but there are insufficient data related to prolonged survival in pulmonary diseases.

Age has not been reported as a criterion in the use indications for domiciliary NIMV. Current data have shown an increase in the elderly population, especially in people of advanced age (74-85 years and ≥ 85 years) [8]. The restriction in the respiratory reserve due to aging and the presence of underlying diseases (COPD, asthma, bronchiectasis, infections,

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neuromuscular diseases, and kyphoscoliosis) in patients of very advanced age causes an increase in CRF, decrease in the QoL, and increased hospital admissions and healthcare costs [9]. The efficacy, safety, and benefits of domiciliary NIMV treatment in patients aged over 75 years with CRF have been reported along with the emphasis on the difficulty of compliance with the treatment, and the failure and risk of neuropsychological impairment, especially in patients aged 80 years and above [8]. In this context, this retrospective, observational, cohort study was planned to determine whether the NIMV treatment was beneficial in a group of elderly patients with CRF and to raise the awareness of physicians about the use of NIMV.

MATERIALS AND METHODS

Design and Study Population

This retrospective, comparative, longitudinal study was conducted in the University of Health Sciences, İstanbul Süreyyapaşa Chest Diseases and Thoracic Surgery Hospital, Pulmonary Intensive Care Outpatient Clinic and included 44 advanced age patients (≥ 80 years old) with stable disease who were referred to the center between 2012 and 2018 to initiate a scheduled domiciliary NIMV. In present study, obstructive lung diseases (chronic obstructive pulmonary diseases [COPD], diagnosed as clinical history, symptoms, and airway obstruction [i.e., forced expiratory volume in 1 second [FEV₁]/forced vital capacity [FVC], 70% of predicted after bronchodilator inhalation[10]) and Restrictive lung diseases (spirometry test showed restriction (FEV₁/FVC over 70% and FVC less than 60% and when lung parenchyma was defective due to tuberculosis sequels or bronchiectasis, which caused hypoventilation and resulted in hypoxemia and hypercapnia [PaCO₂ over 45 mmHg] were compared for long term outcomes.

Definitions and indications of domiciliary NIMV: Domiciliary NIMV was indicated in case of restrictive lung diseases with chronic hypercapnic respiratory failure (CHRF) when symptoms included fatigue, morning headache, dyspnea were present after optimum medical treatment, PaCO₂ daytime findings were over 45 mmHg, and if desaturation was present at sleep (5 minutes continuous saturation with pulse oximeter under 88%). The domiciliary NIMV indications to COPD patients with CHRF were the following: being symptomatic despite an optimal medical treatment (bronchodilators plus steroid and oxygen), PaCO₂ over 55 mmHg or PaCO₂ 50-54 mmHg and nighttime desaturation (i.e., 5 minutes continued observation with nasal cannula under 2 L/min oxygen, saturation less than 88% and over 10% decreasing oxygen saturation during monitoring period), or PaCO₂ 50-54 mmHg, and acute hypercapnic respiratory failure attacks requiring hospitalization more than 2 times per year.

The minimum follow-up period was 6 years from the beginning of the treatment. The participants were separated into two groups, as survivors (n=15) and non-survivors (n=29).

The demographic and clinical characteristic of the groups including age, sex, body mass index (BMI), underlying diseases, pulmonary function, baseline blood gas analysis, and laboratory parameters were recorded together with the duration

of domiciliary NIMV, NIMV compliance, date of death, and survival status. The "baseline" means that the values of arterial blood gases were recorded at the first 2 months after use of domiciliary NIMV.

Patients with idiopathic pulmonary fibrosis, rheumatologic diseases, collagen vascular diseases, active tuberculosis, lymphoma, lung cancer, and patients under the age of 80 were excluded from the study. We also excluded patients who had a short time follow-up period.

The study protocol was approved by the University of Health Sciences, İstanbul Süreyyapaşa Chest Diseases and Thoracic Surgery Hospital Scientific Ethics Committee (Date: 2018/07/12 No: 046). This study was conducted in accordance with the principles of the Declaration of Helsinki. Oral or written informed consent was not taken from the participants for the use of medical data for publication purposes since it was waived by the institution's ethics committee due to the retrospective nature of the study, in line with local legislation.

Statistical Analysis

Statistical analysis was conducted using the IBM Statistical Package for the Social Sciences version 21.0 software (IBM SPSS Statistics Corp.; Armonk, NY, USA). The normal distribution of the data was tested using the Shapiro-Wilk test, and a descriptive study was applied to the variables to be analyzed. Differences between the groups were assessed by the Mann-Whitney U test for continuous data and Fisher's exact test for categorical data. The intragroup comparisons were assessed using the Wilcoxon test for paired samples. The results were presented as median (IQR1-IQR3) values or as number (n) and percentage (%). A significance level was set to 0.05 or lower. Long-term survival was calculated over a 6-year period (beginning from discharge) by Cox regression analysis using the log-rank test. The Kaplan-Meier survival analysis was used to estimate plot survival curves.

RESULTS

Forty-four patients were included into the study, 23 (51.1%) were males, and 21 (48.9%) were females (mean age, 82.6 \pm 2.2 years; range, 80-89 years). The obstructive and restrictive patients' numbers were 21 and 23, respectively. The patients were allocated into two groups according to outcome: survivors group (n=15) and non-survivors group (n=25). The average age of the patients in each group was 82.8 \pm 2.6 years (median, 82 years) in the survivors group and 82.4 \pm 2.0 years (median, 82 years) in the non-survivors group. The median follow-up time was 890 days (interquartile range, 802-1684 days) after NIMV in the survivors group, and 737 days (interquartile range, 472-1146 days) in the non-survivors group (p=0.025). There was no significant difference found between the groups with respect to age, sex, BMI, domiciliary NIMV compliance, biomass smoke exposure, smoking status, the number of comorbid conditions, and the presence of several diseases (all p>0.05). The demographic and clinical data of the surviving and non-surviving patients are summarized in Table 1.

Table 1. Characteristics of all patients aged 80 years or older managed with domiciliary NIMV according to the survival status

Characteristics	All (n=44)	Survivors (n=15)	Non-survivors (n=29)	*p
Age (years)	82 (81-83)	82 (80-84)	82 (81-83)	0.68
Gender, Male/Female	23 (52.3%)/21 (47.7%)	8 (53%)/7 (47%)	15 (52%)/14 (48%)	0.92
Body mass index (kg/m2)	26 (24-30)	25 (24-32)	26 (24-29.5)	0.89
Duration of domiciliary NIMV (d)	828 (529-1287)	890 (802-1684)	737 (472-1146)	0.025
Domiciliary NIMV compliance (≥4h/day)	36 (81.8%)	13 (86.6%)	23 (79.3%)	0.55
Biomass smoke	13 (29.5%)	6 (40%)	7 (24.1%)	0.27
Smoking history	22 (50%)	7 (46.7%)	15 (53.6%)	0.67
Current smoker	1 (2.2%)	0 (0)	1 (3.4%)	0.47
Comorbid conditions	36 (81.8)	10 (66.7%)	26 (89.6%)	0.06
Disease				
Post-tuberculosis sequelae	2 (4.5%)	0 (0)	2 (6.9%)	0.30
Bronchiectasis	3 (6.8%)	1 (6.7%)	2 (6.9%)	0.98
Diabetes mellitus	10 (22.7%)	2 (13.3%)	8 (27.6%)	0.29
Hypertension	22 (50%)	8 (53.3%)	14 (48.3%)	0.75
Atrial fibrillation	6 (13.6%)	2 (13.3%)	4 (13.8%)	0.97
Coronary heart disease	10 (22.7%)	2 (13.3%)	8 (27.6%)	0.29
Cor pulmonale	12 (27.3%)	3 (20%)	9 (31.0%)	0.44
Depression	2 (11.4%)	1 (6.7%)	4 (13.8%)	0.48

Data were given as median (Q1-Q3) or n (%). Bold value shows statistically significant p-values (p<0.05)

*Mann-Whitney U test or chi-squared test were used

NIMV: non-invasive mechanical ventilation

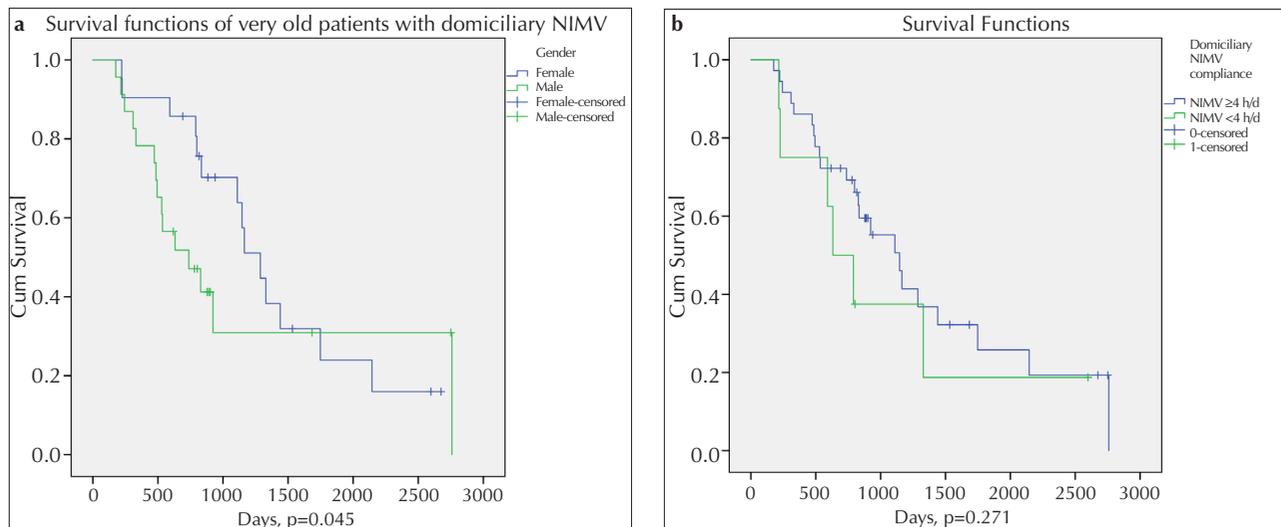


Figure 1. a, b. Kaplan-Meier survival curves in patients with chronic respiratory failure using domiciliary NIMV, with gender and non-invasive mechanical ventilation

NIMV: non-invasive mechanical ventilation; ICU: intensive care unit

A significant difference was found in the hemoglobin level between the groups, with the non-survivors group showing higher hemoglobin levels compared to the survivors group at baseline (p=0.004). No statistically significant difference was determined between the groups and in the within-group comparisons with respect to the pulmonary function tests and blood gas analyses results. The data are presented in Table 2. Compliance was moderate in this elderly population, at 4.9±1.9 h/day (range, 0.8-9.1 h/day). The overall mortality rate was 65.9%. Figure 1 shows a survival analysis related to

sex and NIMV compliance (p=0.045 and p=0.271, respectively).

Table 3 shows the number of intensive care unit (ICU) and ward hospitalizations before the NIMV prescription and after the first year of NIMV use. Twenty-four out of 39 elderly patients of 24 out of 39 were hospitalized once and more than once in the ward, and these numbers were reduced to eight patients out of 39 after 1 year of NIMV use. Among 39 elderly patients of 23 were hospitalized once and more than

Table 2. Comparison of the laboratory data, pulmonary function tests, and blood gas analysis between both groups (at baseline and follow-up)

Characteristics	Baseline			Follow-Up		
	Survivors (n=15)	Non-survivors (n=29)	*p	Survivors (n=15)	Non-survivors (n=29)	*p
Laboratory data						
Hemoglobin (g/L)	11.1 (9.7-11.9)	12.9 (11.7-14)	0.004	12.0 (11-13)	12 (11.6-15)	0.50
Hematocrit (%)	37 (35.4-38)	39.3 (36-45)	0.10	38 (36-42)	37.5 (35-46)	0.97
Pulmonary function tests						
FEV ₁ (ml)	580 (450-700)	560 (350-895)	0.49	505 (350-872)	545 (432-767)	0.69
FEV ₁ (% predicted)	34 (24-57)	33 (23-40)	0.38	32 (22-44.7)	32.5 (18.7-44.5)	0.90
FVC (ml)	1030 (570-1370)	880 (485-1410)	0.57	970 (392.5-1240)	865 (600-1077)	0.93
FVC (% predicted)	40 (35-59)	38 (25-47)	0.28	42.5 (20-48)	36.5 (27-45.7)	0.88
FEV ₁ /FVC (% predicted)	68 (49-78)	72 (61-73)	0.64	70.5 (53.7-75.25)	71.5 (57.7-73.7)	0.98
FiO ₂ (%)	21 (21-21)	21 (21-21)	0.51	21 (21-32)	21 (21-26.5)	0.72
Blood gas analysis						
Ph	7.36 (7.0-7.4)	7.40 (7.35-7.44)	0.07	7.0 (7.0-7.4)	7.38 (7.0-7.4)	0.18
PaCO ₂ (mmHg)	48 (42-58)	47 (43.5-52)	0.63	45 (40-49)	45 (40-64.5)	0.59
PaO ₂ (mmHg)	66 (57-82)	62 (54.5-88)	0.80	69 (60-74)	70 (62-89)	0.57
HCO ₃ (mmol/L)	28.1 (26-33)	28 (26.3-31.7)	0.93-	28.2 (25-30)	29 (28-32)	0.11
BE (mmol/L)	4.7 (2.4-6.0)	4.4 (2.6-7.3)	0.97-	3.5 (1.0-5.3)	5.0 (4.0-7.0)	0.055
SpO ₂ (%)	94 (90-97)	93 (86.5-97.5)	0.72	94 (92-96)	93 (92-96)	0.78

Data were given as median (Q1-Q3) or n (%).value set in bold statistically significant p-values (p<0.05). *Mann-Whitney U Test was used. Wilcoxon's test comparing values at baseline and at the end of follow-up NIMV (all p>0.05).

PaO₂: oxygen pressure in arterial blood; PaCO₂: carbon dioxide pressure in arterial blood; HCO₃: plasma bicarbonate; BE: base excess; SpO₂: oxyhemoglobin saturation by pulse oximeter; FVC: forced vital capacity; FEV₁: forced expiratory volume in 1 sec

Table 3. The numbers of hospitalization pre- and post-domiciliary NIMV use in elderly patients with chronic respiratory failure

	Patients, n (%)	
Pre-domiciliary NIMV, ward numbers admission	None	15 (39)
	1	14 (36)
	2	6 (15)
	3	4 (10)
Pre-domiciliary NIMV, ICU numbers admission	None	15 (40)
	1	17 (45)
	2	5 (13)
	3	1 (3)
First year of domiciliary NIMV, ward numbers admission	None	24 (75)
	1	7 (22)
	5	1 (3)
First year of domiciliary NIMV, ICU numbers admission	None	23 (72)
	1	8 (25)
	3	1 (3)

once in the ICU, and these numbers were reduced to -9 after 1 year of NIMV (Table 3).

DISCUSSION

The main findings of the current research were that the number of comorbid conditions, pulmonary function test, and blood gas analysis did not differ between groups. From the retrospective analysis of these 44 cases, the survivors were found to have a significantly longer duration of domiciliary NIMV (737 days vs. 890 days, p=0.027) and a lower hemoglobin concentration (11.3 g/L vs. 12.7 g/L, p=0.004). Compliance was found to be at a moderate level in this elderly population at 4.9±1.9 h/day (range, 0.8-9.1 h/day). NIMV was well-tolerated in 36 of the 44 elderly patients (81.8%). The overall mortality rate was 65.9%.

Domiciliary NIMV is an effective long-term management, which is being increasingly used in individuals with CRF secondary to a number of heterogeneous conditions. In recent years, domiciliary NIMV programs were developed, and technological advances have enabled an increase in the number of patients treated with domiciliary NIMV. The implementation of an HMV program aims to bring NIMV into the patients' home whenever possible [1]. For patients with CRF, especially those with CHRF, it is extremely important to continue NIV at home, following discharge. The number of emergency department visits due to an attack has been observed to be reduced, and life was prolonged with these applications.

The most frequent reason for restrictive CRF in the elderly is chest wall disorders. Another significant etiology is obe-

sity, which is increasingly becoming more common in all age groups. In elderly population with associated parenchymal diseases, such as sequelae of tuberculous, bronchiectasis is generally present. On the other hand, long-term NIMV treatment is not restricted by age, and indications for long-term NIMV treatment for elderly patients are not different from those of younger patients [11].

There are limited data available related to the home application of NIMV in elderly patients. In a study by Farrero et al. [12] including 43 patients with CHRF who began home ventilation at the age of 75 years or older, the diagnoses of the patients were as follows: 25% had kyphoscoliosis, 33% sequelae of tuberculosis, 21% neuromuscular disease, 19% hypoventilatory disorders, and 2% had a bronchiectasis-kyphosis combination. The results of the study demonstrated that NIMV was effective for these elderly patients in terms of improved arterial blood gases and nocturnal desaturations, and fewer hospital admissions. In our series of 44 patients, sequelae of tuberculosis were determined in 2 (4.5%) patients and bronchiectasis in 3 (6.8%) patients.

Compliance and tolerance have been evaluated in several studies in the literature. In a retrospective comparative study of 110 CHRF patients, Muñoz et al. [13] reported that objective compliance at 1 year after initiating ventilation was 8.6 ± 2.4 h/day for the assist-control ventilation mode group and 8.9 ± 1.6 h/day for the control group. The short-term and long-term advantage of domiciliary NIMV in patients aged ≥ 65 years were evaluated by Crespo et al. [14], and compliance was found to be 8.8 ± 2.2 h/day in the age group of ≥ 75 years old, 9.8 ± 2.3 h/day in the age group of 65-74 years, and 9.5 ± 2.1 h/day in the age group of < 65 years. The results of that study showed no significant differences between the groups with respect to the treatment compliance, and they concluded that domiciliary NIMV is effective in all patients for whom it is indicated, regardless of age. In another study, Farrero et al. [12] reported compliance to be 8.3 ± 3.1 h/day in patients aged 75 years or older. Domiciliary NIMV compliance in advanced age patients has been shown to be relatively low compared to patients aged who were 65 years old or younger, and the results of the current study are consistent with this compliance rate of 4.9 ± 1.9 h/day (range, 0.8-9.1 h/day) in this very elderly population. In our cohort, when examined according to the groups, good NIMV compliance was determined at the rate of 86.6% in survivors, and 79.3% in non-survivors. No statistically significant difference was found between the groups with respect of compliance.

Janssens et al. [15] evaluated tolerance, compliance, and the impact on the QoL of domiciliary NIMV in patients older than 75 years, and an improvement was determined in blood gas levels and QoL following the initiation of domiciliary NIMV. Hazenberg et al. [16] found an improvement in PaCO₂ levels in both hospital and home groups, together with significant improvements in the QoL in both groups. Advanced age is clearly a poor marker of the potential response to HMV. Although domiciliary NIMV can be considered to improve abnormal gas exchange and reduce the number of hospital admissions for elderly patients, the findings of the current study showed that the use of domiciliary NIMV in patients

with respiratory failure did not significantly change the blood gas analysis (PaO₂, PaCO₂, HCO₃⁻, BE, SpO₂) values in both groups at follow-up.

It can be very difficult or sometimes impossible to obtain meaningful pulmonary function test data from elderly patients due to a diminished cognitive function and decreased motor activity [17]. It is also known that the respiratory response to hypoxia and hypercapnia decreases in the older population. Reduced mucociliary clearance in elderly population may be the reason for complications in the NIMV treatment. In addition to aging-related physiological changes in the respiratory system, comorbidities (cardiovascular, neurological, and infectious diseases), the presence of acute conditions (malnutrition, delirium), and a history of pulmonary disease may all predispose to respiratory failure [18]. The results of the pulmonary function tests before the initiation of domiciliary NIMV and at the time of the study are presented in Table 2. There were no significant improvements in FEV₁, FVC, FEV₁/FVC, and FiO₂ in both groups. These results differ from those of many previous studies of spirometry quality in the elderly probably due to the fact that the current study cohort consist of patients aged ≥ 80 years, whereas several previously published studies included younger patients (aged ≥ 65 years). Paone et al. [19] studied the effect of a long-term NIMV on pulmonary and systemic inflammatory response in stable COPD patients with NIMV plus long-term oxygen therapy (LTOT) compared with stable COPD patients with LTOT alone. They found a significant reduction in re-hospitalization after using long-term NIMV plus LTOT (median numbers 2.5 [1-4] versus 1 [0-2], $p < 0.01$). This study also showed that the numbers of re-hospitalization of ICU and wards after domiciliary NIMV plus LTOT were decreased nearly 3 times in elderly patients with NIMV and LTOT in different diseases in first year (Table 3).

The current study has some limitations. First, the primary study limitation is its retrospective design. Second, due to the single-centered design of this study, it seems difficult to establish the temporality between the cause and effect, and to generalize our findings to the very old population. Nevertheless, despite these limitations, when we consider the limited data on long-term follow-up and surveillance data of domiciliary NIMV use in advanced age patients, our results may represent a valuable contribution to the literature.

In conclusion, domiciliary NIMV can be useful for elderly patients, and age is not a restriction factor for domiciliary NIMV use. Therefore, advanced age patients should not be excluded from this treatment on the basis of age alone.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of the University of Health Sciences, İstanbul Süreyyapaşa Chest Diseases and Thoracic Surgery Hospital (Date: 2018/07/12 No: 046).

Informed Consent: Due to the retrospective design of the study, informed consent was not taken.

Peer-review: Externally peer-reviewed.

Conflict of Interest: The author have no conflicts of interest to declare.

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