

The Effect of Recruitment Maneuvers on Dead Space in Patients with ARDS: Prospective Observational Study

ARDS Hastalarında Recruitment Manevralarının Ölü Boşluk Üzerine Etkisi: Prospektif Gözlemsel Çalışma

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ABSTRACT

Objective: Acute Respiratory Distress Syndrome (ARDS) is characterized by severe hypoxemia and heterogeneous lung involvement. Recruitment maneuvers (RMs) and positive end-expiratory pressure (PEEP) titration are commonly employed strategies in lung-protective ventilation to reopen collapsed alveoli and improve oxygenation. However, the effect of these strategies on dead space—a key indicator of ventilation-perfusion mismatch—remains underexplored. This study aimed to investigate the impact of RMs and PEEP titration on dead space in patients with ARDS.

Material and Method: This prospective observational study included twelve early-phase ARDS patients. After initial stabilization, each patient underwent a standard RM protocol followed by decremental PEEP titration. Dead space parameters, lung mechanics, blood gases, and hemodynamic variables were measured before and after RM and individualized PEEP titration.

Results: A statistically significant reduction in both airway and physiological dead space was observed following RM. PaO₂ and oxygen saturation increased, while arterial pH decreased modestly. Alveolar dead space, compliance, airway pressures, end-tidal CO₂, and hemodynamics did not change significantly.

Conclusion: Individualized ventilation strategies with RMs and PEEP may reduce physiological dead space and improve oxygenation in early ARDS without causing significant hemodynamic compromise. These findings suggest that incorporating dead space monitoring could be considered in personalized approaches to help optimize gas exchange and potentially improve clinical outcomes.

Keywords: Acute Respiratory Distress Syndrome (ARDS), dead space, recruitment maneuver, PEEP, mechanical ventilation, respiratory mechanics, ventilation-perfusion ratio.

ÖZET

Amaç: Akut Solunum Sıkıntısı Sendromu (ARDS), şiddetli hipoksemi ve heterojen akciğer tutulumuyla karakterizedir. Rekrütman manevraları (RM) ve pozitif son ekspirum basıncı (PEEP) titrasyonu, kollabe alveollerin yeniden açılmasını sağlamak ve oksijenasyonu artırmak amacıyla akciğer koruyucu ventilasyon stratejileri kapsamında yaygın olarak kullanılmaktadır. Ancak, bu stratejilerin ventilasyon-perfüzyon uyumsuzluğunun önemli bir göstergesi olan ölü boşluk üzerine etkisi yeterince araştırılmamıştır. Bu çalışmanın amacı, RM ve PEEP titrasyonunun ARDS'li hastalarda ölü boşluk üzerine etkisini değerlendirmektir.

Gereç ve Yöntem: Bu prospektif gözlemsel çalışmaya erken evre ARDS tanısı almış on iki hasta dahil edilmiştir. Başlangıç stabilizasyonunun ardından, tüm hastalara standart bir RM protokolü uygulanmış ve ardından azalan PEEP titrasyonu gerçekleştirilmiştir. RM ve bireyselleştirilmiş PEEP titrasyonu öncesi ve sonrasında ölü boşluk parametreleri, akciğer mekaniği, kan gazları ve hemodinamik değişkenler ölçülmüştür.

Bulgular: RM sonrasında hem hava yolu ölü boşluğu hem de fizyolojik ölü boşlukta istatistiksel olarak anlamlı bir azalma gözlenmiştir. PaO₂ ve oksijen saturasyonu artarken, arteriyel pH'ta hafif bir düşüş saptanmıştır. Alveoler ölü boşluk, kompliyans, hava yolu basınçları, son-tidal CO₂ ve hemodinamik parametrelerde ise anlamlı bir değişiklik izlenmemiştir.

Sonuç: Erken dönem ARDS'de, RM'ler ve PEEP ile uygulanan bireyselleştirilmiş ventilasyon stratejileri, belirgin bir hemodinamik bozulmaya yol açmadan fizyolojik ölü boşluğu azaltabilir ve oksijenasyonu iyileştirebilir. Bu bulgular, gaz değişimini optimize etmeye yardımcı olmak ve klinik sonuçları potansiyel olarak iyileştirmek amacıyla, kişiselleştirilmiş yaklaşımlara ölü boşluk monitörizasyonunun dahil edilebileceğini düşündürmektedir.

Anahtar Kelimeler: Akut solunum sıkıntısı sendromu (ARDS), ölü boşluk, recruitment manevrası, PEEP, mekanik ventilasyon, solunum mekaniği, ventilasyon-perfüzyon oranı.

INTRODUCTION

Acute respiratory distress syndrome (ARDS) is a life-threatening condition characterized by acute-onset respiratory failure with severe hypoxemia, typically triggered by underlying causes such as pneumonia, sepsis, or trauma (1–4). In ARDS, a profound inflammatory process disrupts the alveolar-capillary barrier, increases vascular permeability,

and leads to alveolar collapse and diffuse alveolar damage (5). These pathophysiological changes result in impaired gas exchange, reduced lung compliance, and the development of non-cardiogenic pulmonary edema (6).

The primary goal in the management of ARDS is to improve oxygenation while minimizing ventilator-induced lung injury (VILI). Lung-protective ventilation (LPV) strategies,

particularly the use of low tidal volumes and appropriate levels of positive end-expiratory pressure (PEEP), form the cornerstone of ARDS management. Following the ARDS Network trial, which demonstrated reduced mortality with LPV, these strategies have become standard clinical practice (7). Current guidelines recommend mechanical ventilation using a tidal volume of approximately 6 mL/kg of predicted body weight, limiting plateau pressures to ≤ 30 cmH₂O, and applying higher PEEP levels and recruitment maneuvers (RMs) in selected patients (8–9). RMs are brief, controlled increases in airway pressure aimed at reopening collapsed alveoli, thereby improving oxygenation by increasing end-expiratory lung volume (10). PEEP titration is an essential component of individualized ventilation strategies and seeks to identify the optimal PEEP that maintains alveolar recruitment without causing overdistension (11).

Dead space (VD) refers to ventilated but non-perfused lung regions that do not participate in gas exchange, thereby reducing respiratory efficiency (12–14). In ARDS, the dead space ratio (VD/VT – the ratio of dead space volume to tidal volume) is frequently elevated due to ventilation-perfusion (V/Q) mismatch and impaired pulmonary perfusion (15). Pulmonary microvascular injury, thrombosis, and regional hypoperfusion contribute to increased dead space, impairing CO₂ elimination. These findings suggest that dead space fraction may serve as a reliable marker for evaluating lung function and ventilation in ARDS patients.

Although RMs can improve oxygenation in ARDS patients with refractory hypoxemia, their impact on respiratory mechanics and dead space ventilation is less well defined (16–17).

The aim of this study is to evaluate the effect of RMs and PEEP titration on dead space and gas exchange in ARDS.

MATERIAL AND METHOD

This prospective observational study was conducted in the Sadi Sun Intensive Care Unit (ICU) Istanbul University-Cerrahpaşa, Cerrahpaşa Medical School, following approval by the Ethics Committee (2004-14523) and after obtaining informed consent from the patients or their legal representatives. Patients who met the diagnostic criteria for ARDS were included in the study (1-4). Patients diagnosed with chronic obstructive pulmonary disease (COPD), who were receiving bronchodilator therapy, as well as children under 14 years of age were excluded.

Patients who were orotracheally intubated received mechanical ventilation (MV) with a Servo 300a ventilator (Siemens, Solna, Sweden) in Pressure Regulated Volume Control (PRVC) mode. Ventilation settings were as follows: tidal volume (TV): 6 mL/kg, inspiratory/expiratory ratio (I:E): 1:2, PEEP: +10 cmH₂O, fractional inspired oxygen (FiO₂) <0.6, oxygen saturation >90%, and pH>7.25.

After stabilization of hemodynamic and respiratory parameters, baseline measurements were taken at the bedside. Volumetric capnography is defined as the simultaneous measurement of flow using a pneumotachograph and carbon dioxide with a capnograph from expired air. When combined with arterial PCO₂ (PaCO₂) measurements, it allows for precise calculation of the VD/VT ratio. Simultaneous monitoring of airflow and CO₂ provides information on CO₂ production and pulmonary dead space on a breath-by-breath basis and is referred to as the Single Breath Test (SBT) (13). After calibration, the Ventrak (Model 1550 Respiratory Monitor, Novometrix Medical Inc. USA) and CO₂SMO (EtCO₂ and SpO₂ monitor, Novometrix

Medical Systems Inc., Wallingford, CT, USA) devices were used to obtain baseline measurements and to measure dead space via “volumetric capnography.”

Airway dead space (VDaw) was calculated using the Fowler method (13), and physiological dead space (VDphys) was calculated using the Enghoff modification of the Bohr equation as follows (12): $VD_{phys} = (PaCO_2 - PAECO_2) / PaCO_2 \times VT$

Here, PAECO₂ represents the average partial pressure of alveolar carbon dioxide in the expired air (14).

Following the recording of dead space, dynamic lung compliance (C_{dyn}), peak airway pressure (P_{peak}), mean airway pressure (P_{mean}), end-tidal CO₂ (EtCO₂), and arterial blood gas values (PaO₂, PaCO₂, arterial pH, and O₂ saturation), the patient received sedation and neuromuscular blockade. A recruitment maneuver was then performed in CPAP mode with 100% FiO₂, using a sustained inflation technique at 45 cmH₂O for 45 seconds (18).

After the RM, PEEP titration was performed. Ventilator settings were adjusted to PRVC mode, TV: 6 mL/kg, FiO₂: 100%, PEEP: 18 cmH₂O, and pH>7.25. PEEP was titrated by decreasing it from 18 cmH₂O in 2 cmH₂O steps. At each PEEP level, the patient was ventilated for 10 minutes of stabilization preceded measurements. During the procedure, systolic arterial pressure (SAP), diastolic arterial pressure (DAP), and heart rate (HR) were monitored via invasive arterial monitoring and recorded.

The optimal PEEP was defined as the highest PEEP level just before the onset of decreased oxygen saturation, where oxygenation was best and hemodynamics was least affected. The RM was repeated after titration, and MV was continued using the optimal PEEP value. Dead space and other lung mechanics measurements were then repeated.

Following the recruitment maneuver and the establishment of optimal positive end-expiratory pressure (PEEP), a stabilization period of 30 minutes was strictly observed (19). This equilibration phase was mandated to ensure the restoration of hemodynamic stability and the complete physiological adaptation of alveolar mechanics. All post-intervention measurements, including arterial blood gas analyses and the assessment of respiratory mechanics, were exclusively recorded after this steady-state was achieved.

During patient follow-up, in cases of oxygenation deterioration such as sudden SpO₂ drop, the need to disconnect the ventilator (e.g., for aspiration), or the detection of new crackles on auscultation, measurements were repeated prior to RM, and the RM was performed in accordance with the protocol. Measurements were performed initially after ARDS diagnosis and then again next day nearly 12–18 hours later. Parameters obtained before and after the RM were recorded and compared.

All physiological measurements and data acquisition were carefully carried out by the attending intensive care specialist managing the patient. Respiratory mechanics and gas exchange parameters were recorded directly from the mechanical ventilator and point-of-care blood gas analyzers. Due to the clinical nature of the recruitment maneuvers and the necessity for real-time patient monitoring during optimal PEEP titration, observer blinding was not feasible during the data collection phase. However, all data extraction followed a strict, standardized protocol to ensure objectivity.

For statistical analysis, parametric data were analyzed using the paired Student's t-test, and non-parametric data using the

Table 1: Patient Characteristics.

Variable	Result (mean ± SD)
Age (years)	65 ± 15.64
APACHE II	29.3 ± 8
LIS	2.6 ± 0.35

APACHE II: Acute Physiology and Chronic Health Evaluation II, LIS: Lung Injury Score, SD: Standard deviation

Table 2: ARDS Etiologies.

	Male (n=8)	Female (n=4)
Pneumonia	1	1
Trauma	1	-
Sepsis	6	3

Kruskal-Wallis test. Results are presented as mean ± standard deviation (SD), and $p < 0.05$ was considered statistically significant.

RESULTS

A total of 12 patients diagnosed with ARDS (8 males, 4 females) were included in our study. The mean age was 65 ± 15.6 years. Upon hospital admission, the mean Acute Physiology and Chronic Health Evaluation II (APACHE II) score was 29.3 ± 8.0 , and the mean Lung Injury Score (LIS) was 2.6 ± 0.35 , indicating moderate to severe lung injury (Table 1). The most common etiology of ARDS was sepsis (75%); other causes included pneumonia ($n=2$) and trauma ($n=1$) (Table 2).

Although numerical decreases were noted after the RM,

importantly, no statistically significant changes were observed in alveolar dead space ($V_{D\text{alv}}$) (from 76.79 ± 56.25 mL to 58.04 ± 51.10 mL; $p=0.18$). Likewise, the change in airway dead space ($V_{D\text{aw}}$) (from 119.12 ± 30.49 mL to 116.28 ± 32.00 mL; $p=0.33$) did not reach statistical significance (Table 3).

In arterial blood gas analysis, significant changes were observed before and after RM. PO_2 increased from 108.38 ± 35.64 mmHg to 140.42 ± 58.60 mmHg ($p=0.01$); SAO_2 increased from $96.16 \pm 2.54\%$ to $97.51 \pm 2.01\%$ ($p=0.02$); and pH decreased from 7.30 ± 0.10 to 7.28 ± 0.12 ($p=0.006$). The change in PCO_2 was not statistically significant ($p=0.31$) (Table 4).

The end-tidal carbon dioxide ($EtCO_2$) value was 42.78 ± 6.24 mmHg before RM and 44.61 ± 5.48 mmHg after RM, with no statistically significant difference ($p=0.11$).

In lung mechanics measurements before and after recruitment, dynamic compliance (C_{dyn}) was 30.54 ± 6.8 mL/cmH₂O and 31.66 ± 7.16 mL/cmH₂O, respectively ($p=0.14$); peak airway pressure (P_{peak}) was 27.64 ± 3.27 cmH₂O and 27.95 ± 3.28 cmH₂O ($p=0.61$); and mean airway pressure (P_{mean}) was 15.47 ± 2.20 cmH₂O and 16.98 ± 8.38 cmH₂O ($p=0.40$). These differences were not statistically significant.

The initial PEEP value set at the beginning of mechanical ventilation was 10.67 ± 1.85 cmH₂O, and the optimal PEEP value determined after RM and titration was 11.56 ± 2.85 cmH₂O. This difference was not statistically significant ($p=0.08$).

No significant changes were observed in hemodynamic parameters during the procedure (Table 5).

DISCUSSION

In this prospective observational study, we evaluated the impact of RMs and individualized PEEP titration on dead

Table 3: Changes in Dead Space Values.

	Pre-RM (mean ± SD)	Post-RM (mean ± SD)	p-value
$V_D/V_{T\text{aw}}$	0.27 ± 0.09	0.26 ± 0.08	0.028*
$V_D/V_{T\text{phys}}$	0.49 ± 0.14	0.40 ± 0.10	0.008*
$V_{D\text{phys}}$ (mL)	198.25 ± 60.76	168.10 ± 44.54	0.04*
$V_{D\text{alv}}$ (mL)	76.79 ± 56.25	58.04 ± 51.10	0.18
$V_{D\text{aw}}$ (mL)	119.12 ± 30.49	116.28 ± 32	0.33

RM: Recruitment maneuver; $V_D/V_{T\text{aw}}$: Airway dead space ratio, $V_D/V_{T\text{phys}}$: Physiological dead space ratio, $V_{D\text{phys}}$: Physiological dead space, $V_{D\text{alv}}$: Alveolar dead space, $V_{D\text{aw}}$: Airway dead space, $p < 0.05$ indicates statistical significance.

Table 4: Changes in Arterial Blood Gas Values.

	Pre-RM (mean ± SD)	Post-RM (mean ± SD)	p-value
PO_2 (mmHg)	108.38 ± 35.64	140.42 ± 58.60	0.01*
PCO_2 (mmHg)	50.62 ± 9.59	52.32 ± 8.77	0.31
pH	7.30 ± 0.10	7.28 ± 0.12	0.006*
O ₂ Saturation (%)	96.16 ± 2.54	97.51 ± 2.01	0.02*

PO_2 : Partial pressure of oxygen, PCO_2 : Partial pressure of carbon dioxide, RM: Recruitment maneuver, $p < 0.05$ indicates statistical significance

Table 5: Hemodynamic Changes.

	Pre-RM (mean ± SD)	Post-RM (mean ± SD)	p-Value
Systolic BP (mmHg)	106.72 ± 24.49	102.94 ± 23.61	0.30
Diastolic BP (mmHg)	57.56 ± 15.91	57.72 ± 14.40	0.91
Heart Rate (beats/min)	103.39 ± 13.92	102.28 ± 14.47	0.22

Systolic BP: Systolic blood pressure; Diastolic BP: Diastolic blood pressure; HR: Heart rate, RM: Recruitment maneuver, $p < 0.05$ indicates statistical significance.

space parameters, gas exchange, and lung mechanics in patients with early-phase ARDS. Our findings demonstrated a statistically significant reduction in both airway and physiological dead space following the application of RM and PEEP titration. In parallel, improvements in oxygenation parameters such as PaO₂ and arterial oxygen saturation were observed, while pH decreased slightly but remained within acceptable clinical limits. Importantly, these interventions did not result in significant changes in alveolar dead space, lung compliance, airway pressures, or hemodynamic parameters.

These results suggest that early application of RMs combined with individualized PEEP titration may contribute to improved ventilation-perfusion (V/Q) matching by reducing physiological dead space, which is often elevated in ARDS due to pulmonary microvascular injury, regional hypoperfusion, and alveolar derecruitment. From a clinical standpoint, lowering dead space enhances CO₂ elimination efficiency and may reduce the burden of mechanical ventilation by promoting more effective alveolar ventilation without increasing ventilator pressures or compromising hemodynamic stability. Thus, in selected ARDS patients, integrating recruitment maneuvers into a lung-protective ventilation strategy may offer meaningful physiological and potentially prognostic benefits.

In ARDS and acute lung injury (ALI), these microvascular-level changes have been shown to increase physiological dead space, which is associated with worse prognosis (20). In a meta-analysis by Jayasimhan et al. (21), a significant association between the VD/VT ratio and hospital mortality was demonstrated, and the prognostic value of early dead space measurement was emphasized. Consistent with the literature, our physiological findings align with the concept that high dead space ratios could be indicative of poor clinical trajectories, highlighting the importance of early monitoring. Nuckton et al. (15) reported that high early dead space ratios in ARDS patients were associated with increased mortality. Similarly, Kallet et al. (22) found that in early ARDS, patients with a VD/VT \geq 0.60 had significantly higher mortality, suggesting that this parameter may help identify high-risk patients. These findings suggest that interventions aimed at reducing dead space may improve V/Q matching. Our results align with literature linking dead space reduction to improved gas exchange.

Following the ARDSNet study in 2000 (7), the use of low tidal volume (TV), plateau pressure \leq 30 cmH₂O, prone positioning, high PEEP, and recruitment maneuvers when needed has become standard in ARDS management. In 2017, the American Thoracic Society (ATS), European Society of Intensive Care Medicine (ESICM), and Society of Critical Care Medicine (SCCM) published guidelines recommending these strategies for managing mechanical ventilation (MV) in adult ARDS patients based on evidence (9). These approaches aim to reduce ventilator-induced lung injury (VILI) and lower mortality. In line with these strategies, our study employed a lung-protective ventilation (LPV) strategy using 6 mL/kg TV, plateau pressure $<$ 30 cmH₂O, individualized PEEP, and recruitment maneuvers.

The effect of PEEP on dead space is complex. While positive pressure increases ventilation, especially in the upper lung regions and improves V/Q ratio, it may also increase dead space due to reduced perfusion in these areas. Slobod et al. (23) showed that appropriate PEEP levels could reopen collapsed alveoli and improve V/Q matching; however,

excessive PEEP could impair perfusion via overdistension and capillary compression. Therefore, individualizing and optimizing the PEEP level is critically important.

Blanch et al. (24), in a study evaluating different PEEP levels using volumetric capnography in ALI patients, showed that while increased PEEP improved alveolar ventilation in some patients, it also increased dead space in others. Gogniat et al. (25), in a study applying incremental PEEP levels to ARDS patients and analyzing dead space at each level, found that in some patients, alveolar recruitment at high PEEP reduced dead space, while in others, a $>$ 15% increase in driving pressure was associated with a rise in VD/VT ratio. These findings suggest that the effects of PEEP vary between patients, necessitating a personalized approach for optimal PEEP determination and highlighting the potential utility of dead space monitoring as a clinical guide. In our study, the average PEEP level achieved after RM (11–12 cmH₂O) showed no further significant impact on alveolar dead space compared to the baseline (\sim 10 cmH₂O).

The goal of recruitment maneuvers is to reopen collapsed alveoli and increase the volume of aerated lung, or “baby lung” (16). They may be particularly effective when applied in early ARDS during refractory hypoxemia. In the initial exudative phase of ARDS, when alveoli are largely collapsed but fibrotic changes have not yet developed, reopening is more likely. Applying RM early in ARDS (within the first 72 hours) alongside LPV has been shown to improve outcomes and increase ventilator-free days among survivors (26). A meta-analysis by Cui et al. (27), including 3,025 patients, showed that RMs did not reduce mortality but positively affected oxygenation and length of hospital stay. In our study, a 45-second RM using 45 cmH₂O CPAP was applied to early ARDS patients, resulting in improved oxygenation and a significant reduction in VD/VT ratio. This may be explained by alveolar recruitment, improved V/Q matching, and attenuation of hypoxic pulmonary vasoconstriction. Additionally, adequate sedation and fluid management may have supported hemodynamic stability. The slight post-RM increase in PaCO₂ and decrease in pH likely reflect transient CO₂ retention but remained within acceptable limits.

The aim of PEEP titration is to identify the lowest PEEP level that preserves oxygenation gains after RM without adversely affecting the cardiovascular system. Heunks et al. (28), in patients with acute hypoxemia, adjusted PEEP levels according to the PEEP/FiO₂ table (typically 8–12 cmH₂O), then performed a PEEP response test. PEEP was increased from 5 to 15 cmH₂O, and oxygenation, compliance, and PaCO₂ were assessed. If no significant deterioration occurred, patients were considered potential beneficiaries of higher PEEP. They concluded that PEEP titration should be personalized based on individual patient characteristics and lung recruitability and approached dynamically, guided by physiological responses and clinical monitoring.

Although some studies (29) have proposed determining optimal PEEP based on the lower inflection point of pressure-volume curves, technical challenges and practical limitations have hindered its widespread use. Hickling (30) reported that the decremental PEEP titration method was more effective in maintaining lung recruitment after RM. In our study, we also adopted the decremental PEEP titration approach and observed that the specific PEEP level had no further significant impact on alveolar dead space. The average optimal PEEP level was slightly higher than the baseline, but there was no additional

significant change in the VD/VT ratio during this titration phase. This suggests that moderate PEEP may be sufficient to keep recruited alveoli open without disrupting V/Q balance. Studies evaluating the effect of recruitment maneuvers on dead space are limited. Tusman et al. (31), in an animal model, showed that RM followed by incremental PEEP titration reduced VD/VT until an optimal point, after which excessive PEEP reversed the effect. These data suggest that dead space monitoring could guide PEEP titration. In our study, although physiological dead space was reduced and oxygenation improved in early ARDS patients, we explicitly observed no statistically significant reduction in alveolar dead space. This lack of significant change may be attributed to the complex dynamics of ARDS, where the recruitment of collapsed alveoli might be partially offset by the overdistension of open alveoli. Overall, these findings suggest the potential clinical benefits of individualized ventilation strategies in ARDS management.

Our study has some limitations. Being a single-center study with a limited number of patients restricts the generalizability of the results. Additionally, the study included only early-

stage ARDS patients; results may differ in late-stage ARDS or in patients with different etiologies. Finally, this was a short-term physiological study; long-term clinical outcomes, including survival or duration of mechanical ventilation, were not assessed. Future multicenter trials with larger sample sizes and long-term outcome assessments are needed to validate these findings and explore their prognostic implications. Despite these limitations, our study provides valuable insight into the acute physiological effects of recruitment maneuvers in early ARDS and advocates for considering the integration of individualized strategies.

CONCLUSION

Individualized ventilation strategies—such as recruitment maneuvers and PEEP titration—based on patient-specific characteristics, the stage of the disease, and the prevailing clinical condition, may reduce dead space and improve oxygenation in early ARDS without significant hemodynamic compromise. These findings suggest that incorporating dead space monitoring into personalized approaches could help optimize gas exchange and potentially improve clinical outcomes

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Ethics: Ethics approval was obtained from the Clinical Research Ethics Committee of Istanbul University-Cerrahpaşa (Decision No: 14523, Date: 07.06.2004).

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