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ORIGINAL CONTRIBUTIONS

Preoperative Inspiratory Muscular Training to Prevent Postoperative Hypoxemia in Morbidly Obese Patients Undergoing Laparoscopic Bariatric Surgery. A Randomized Clinical Trial

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Abstract
Background Morbidly obese patients show an increased risk of postoperative hypoxemia and pulmonary complications when compared with normal weight subjects. The purpose of this study was to determine the effects of preoperative inspiratory muscular training (IMT) on postoperative arterial oxygenation in morbidly obese patients submitted to laparoscopic bariatric surgery.
Methods Forty-four morbidly obese patients were randomly assigned to receive either preoperative usual care (control group, n=21) or preoperative IMT (trained group, n=23) for a month prior to the date of surgery. Data on oxygenation (PaO_2/FiO_2 ratio) were obtained at 1 h and at 12 h after surgery (PACU 1 h and PACU 12 h, respectively). Data on maximum static inspiratory pressure (MIP) were obtained before and after the training period, and at postanesthesia care unit (PACU) 12-h time point.
Results PaO_2/FiO_2 was significantly higher in the trained group than in the control group, both at PACU 1 h (305.2±77.6 vs. 248.8±53.8, P=0.008) and at PACU 12 h (333.5±59.6 vs. 289.7±79.6, P=0.044). As a consequence, the percentage of patients with relative hypoxemia (PaO_2/FiO_2 lower than 300 mmHg) at the time of PACU discharge was higher in the control group (57 vs. 17 %, P: 0.006). MIP was significantly higher in the trained group compared with the control group at the preoperative time point (89.87±19.00 vs. 77.00±21.20 cm H_2O, P=0.04).
Conclusions Preoperative IMT improved postoperative oxygenation and increased inspiratory muscular strength in morbidly obese patients submitted to laparoscopic bariatric surgery.

Keywords Obesity · Surgery · Bariatric · Laparoscopy · Respiratory muscle training · Lung · Respiratory function · Postoperative pulmonary complications · Oxygen · Partial pressure

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Introduction

Laparoscopic bariatric surgery has become more popular in the recent years due to its effectiveness [1], low morbimortality, and high patient acceptance [2] [3]. Morbidly obese patients show an increased risk of hypoxemia during the postoperative period despite supplemental oxygen therapy [4]. As a consequence, higher incidence of postoperative pulmonary complications (PPC) and longer length of stay in hospital is observed when compared with normal weight subjects [5] [6]. Respiratory physiotherapy has been suggested in non-bariatric surgery to prevent PPC because of its capacity to induce faster respiratory function recovery, to improve pulmonary volumes and arterial oxygenation, and to decrease postoperative atelectasis, especially after abdominal surgery [7] [8] [9]. It has been demonstrated that preoperative IMT preserves postoperative inspiratory muscle strength following major abdominal surgery [10], and reduces the incidence of PPC after upper abdominal surgery [11], thoracic surgery [12], and CABG surgery [13] [14]. To our knowledge, no studies assessing the effects of preoperative IMT on postoperative respiratory function in morbidly obese patients have been published to date. We designed a double-blinded, parallel-assignment, randomized clinical trial to determine whether a program of preoperative IMT, coupled with incentive spirometry, would improve postoperative oxygenation in morbidly obese patients submitted for laparoscopic bariatric surgery. The primary outcome measure was oxygenation at two time points of the postoperative period. Besides, we measured the effects of IMT on respiratory muscular strength (maximal inspiratory and expiratory pressures, MIP, and MEP, respectively) and spirometric parameters.

Methods

Subjects

Fifty morbidly obese patients (BMI of 40 kg/m^2 or more) who were consecutively scheduled for bariatric surgery from February 2011 to February 2012 and aged between 18 and 60 years were recruited for the study. Exclusion criteria were consent refusal, pregnancy, chronic obstructive pulmonary disease, bronchial asthma requiring regular therapy, smoking less than 2 months before the surgery, severe psychiatric disorders, inability to perform a valid spirometry and/or correctly use IMT and incentive spirometer (IS) devices, restrictive lung disease or lung surgery, cardiac disease associated with dyspnoea (New York Heart Association functional classification II or worse), and obesity–hypercapnia syndrome (OHS). The trial was performed at the Department of Surgery, in the Hospital Clínic Universitari Valencia, Spain. All subjects were treated by the same surgical team and underwent the same general anesthesia procedures. All the patients were explained the aims and interventions of the study and signed informed consent. The protocol was approved by the local human research ethics committee of the hospital (ID: EC-08-2011) and was registered with ClinicalTrialsGov (Identifier: NCT01828632).

Design, Blinding, Randomization, and Interventions

Patients were randomly and blindly assigned to either the control group (CG) or the trained group (TG) using a computer-generated random table of codes and individual closed-sealed envelopes. Surgery was scheduled between days 32 and 34 after the baseline day for all patients. Patients assigned to the TG underwent a program of IMT (Threshold IMT, Respironics Inc. Pittsburgh, PA, USA) and lung re-expansion (Incentive Spirometer, Voldyne5000, Teleflex medical, USA) for 30 consecutive days before surgery. Each daily session consisted of 20 min each of IMT and IS. Initially, the loads were adjusted to 30 % of the MIP and subsequently increased progressively, day by day, when the rates of the Borg scale of perceived exertion [15] were lower than 5. Our team's physiotherapist weekly evaluated the adherence of patients to the IMT program. Patients from both groups were explained the meaning of maximum static pressures and spirometry measurements in order to avoid any learning effects during the study. Anesthetic management was standardized for all patients. In the operating room, patients were placed in the reverse Trendelenburg position (30°). Propofol, remifentanil, and rocuronium were used both for induction and maintenance applying the principles of total intravenous anesthesia (see Supplementary Material, 1). In order to minimize the effects of anesthesia and pneumoperitoneum on the lung volumes, a ventilatory strategy based on continuous pressurization of the airways was applied throughout the intraoperative period (see Supplementary Material, 1). At the end of surgery, tracheal extubation was performed, and the patients were transferred to the postanesthesia care unit (PACU) in a semi-sitting position while receiving a high flow rate (12 L/min^{-1}) of 50 % oxygen in air. This position and oxygen therapy were kept throughout the stay in PACU. Postoperative physiotherapy was the same for both groups and consisted of lung re-expansion exercises with the aid of the IS [16]. Patients were discharged from the hospital on the fifth day after surgery unless there were complications. Any PPC which occurred during the hospital stay, including respiratory failure requiring mechanical ventilation, pneumonia, barotrauma, and atelectasis requiring an intervention such as bronchoscopy, were recorded.

Data Collection and Measurements

Arterial blood gases were measured at four time points: after tracheal intubation (T1), after pneumoperitoneum withdrawal (T2), 1 h after PACU admission (PACU 1 h), and 12 h after PACU admission (PACU 12 h). Pulse oximetry (SpO_2) was recorded continuously throughout the stay in PACU, and the number of episodes of desaturation (SpO_2 less than 90 %) was determined for each patient. FVC, FEV1, MIP, and MEP (Datospir-600D, SIBEL SA, Spain) were measured at three time points: before starting the IMT program (basal), 1 day before surgery (preoperative), and at PACU 12-h time point. MIP was measured from residual volume and MEP from total lung capacity. Five maneuvers were performed for each patient, with the three most acceptable values recorded and the highest used for calculations. Spirometry was performed according to the American Thoracic Society (ATS) recommendations [17], and their results were expressed as a percentage of the normal values calculated according to Knudson et al. [18]. Arterial blood gases, static compliance of the respiratory system (Csr), and end-expiratory lung volume (EELV) measures were obtained in the times T1 and T2 (see Supplementary Material, 2). All the functional data was obtained by the same investigator, who was blinded about to what group each patient had been allocated.

Sample Size Calculation

The sample size was calculated using repeated postoperative PaO_2/FiO_2 measures as the primary end point. We carried out a retrospective analysis of the data from 11 morbidly obese patients previously submitted for laparoscopic bariatric surgery in our department (see Supplementary Material, 3). Assuming a 25 % increase in PaO_2/FiO_2 in the TG (standardized mean difference of 25 %; Cohen's d=0.25), with an apha error probability of 0.05 and a power of 0.95, a sample size of 44 patients would be required (GPower v.3.1.5 program [19]). To account for attrition, we added 15 %, reaching a total sample size of 50.

Statistical Analysis

To compare variables between groups, t test or Mann–Whitney U test (for continuous variables) and χ^2 test or Fisher's exact test (for categorical variables) were used. The paired t test or the Wilcoxon test were applied to compare intragroup data between two time points. Continuous variables were tested for normality using the Kolmogorov–Smirnov test with a Lilliefors' correction. In order to concrete the effect of the time points (PACU 1 h or PACU 12 h) and the group treatment (control or trained) on postoperative PaO_2/FiO_2, a linear mixed effects model was carried out. All data are expressed as mean±standard deviation (SD). All reported P values are two-sided, and P values less than 0.05 were considered statistically significant. All analysis was performed with the statistical software SPSS v.17.0 (SPSS Inc. Chicago, IL, USA).

Results

The enrollment of the patients, randomization, and dropouts were carried out according to the recommendations of the CONSORT statement [20]. Two patients were excluded after the first screening due to latex allergy and OCFA, respectively. After randomization, one patient from the TG and two from the CG were excluded due to violations of the study protocol. Thus, the TG was composed of 23 patients and the CG of 21. At the end of the study, complete data were available for all 44 patients. The basal features did not differ significantly between groups except for the BMI, which was higher in the CG and remained significantly higher at preoperative time point (Table 1). There were no differences between groups in the laparoscopic bariatric procedures. Four patients in each group underwent sleeve gastrectomy, while 19 (82.6 %) in the TG and 17 (79.0 %) in the CG underwent gastric bypass. The mean MIP values did not differ between groups at basal time point, but increased significantly during the training period in the TG and was significantly higher compared to the CG at the preoperative time point (Table 1).

The mean PaO_2/FiO_2 values at PACU 1 h and at PACU 12 h were significantly higher in the TG than in the CG (PACU 1 h: 305.2±77.6 vs. 248.8±53.8, P=0.008; PACU 12 h: 333.5±59.6 vs. 289.7±79.6, P=0.044) (Fig. 1). As a consequence, the percentage of patients with relative hypoxemia (PaO_2/FiO_2 lower than 300 mmHg) was higher in the CG than in the TG at both PACU 1 h (CG 17/21, 81 %; TG 13/23, 57 %; P: 0.06) and PACU 12 h (CG 12/21, 57 %; TG 4/23, 17 %; P: 0.006) (Fig. 2).

From the results of the mixed linear model, PaO_2/FiO_2 postoperative score could be modeled as follows: PaO_2/FiO_2=(252.4+50.5*group)+(33.9*time). In this equation, group and time are dummy variables (group=1 for TG, or 0 otherwise; time=1 for PACU 1 h, or 0 otherwise). Thus, preoperative IMT would increase the postoperative PaO_2/FiO_2 by 20 % (50.5/252.4=0.20) (see Supplementary Material, 4). The total number of episodes of hypoxemia (SpO_2 less than 90 %) was higher in the CG (78) than in the TG (17). No patients from the TG had more than 5 episodes of oxygen desaturation, whereas 6 patients from the CG had between 6 and 31 episodes. There were no differences between groups in $PaCO_2$ values at PACU 1 h (CG 44.4±5.1 vs. TG 41.5±7.7; P=0.167) or at PACU 12 h (CG 40.0±4.6 vs. TG 39.9±5.7; P=0.981).

At PACU 12 h, MIP and MEP were reduced in both groups compared to preoperative values (Fig. 3) and were higher in

Table 1 Basal features and functional data (mean±standard deviation)

	Control group (n=21)	Trained group (n=23)	P value
Sex, male	12 (57 %)	11 (48 %)	0.54
Age, years	43.2±10.9	43.7±9.1	0.86
Smoking, yes	6 (29 %)	7 (30 %)	0.89
Operative time (min)	130±17	132±18	0.71
BMI (kg m^{-2})	51.6±6.9	47.5±4.3	0.02
Basal	48.9±6.8	44.0±5.1	0.01
Preoperative			
FVC (L)	3.45±1.06	3.45±0.70	0.98
Basal	3.39±0.98	3.49±0.65	0.69
Preoperative			
FEV1 (L s^{-1})	2.78±0.77	2.93±0.65	0.50
Basal	2.78±0.75	2.95±0.59	0.39
Preoperative			
MIP (cm H_2O)	76.5±17.0	75.7±18.4	0.88
Basal	77.0±21.2	89.9±19.0	0.04
Preoperative			
MEP (cm H_2O)	106.8±32.7	93.48±29.1	0.16
Basal	102.8±37.5	96.39±28.6	0.52
Preoperative			

FVC forced vital capacity, *FEV1* forced expiratory volume at 1 s, *MIP* maximal inspiratory pressure, *MEP* maximal expiratory

the TG than in the CG, though these differences did not reach statistical significance (MIP 53.3±27.7 vs. TG 58.26±27.6, P=0.35; MEP 63.3±37.4 vs. 72.3±30.9, P=0.14). A post hoc analysis was conducted to determine whether the between-groups difference in BMI at preoperative time point could have had any influence on the main outcome. There was no correlation between the preoperative BMI and the mean PaO_2/FiO_2 in both groups at any of the postoperative time points. In consequence, we concluded that the abovementioned differences in BMI caused no significant effects on the post-operative oxygenation (CG Pearson correlation coefficient P values=0.272 and 0.062, ANOVA 0.543 and 0.123, PACU 1 h and PACU 12 h, respectively; TG Pearson correlation coefficient P values=0.031 and 0.185, ANOVA 0.061 and 0.369, PACU 1 h and PACU 12 h, respectively).

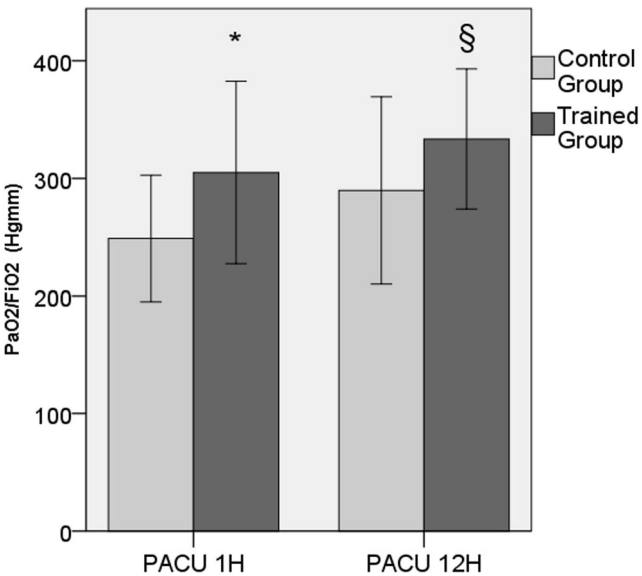

Fig. 1 PaO_2/FiO_2 mean and standard deviation values at the two post-operative time points (PACU 1 h: 1 h after PACU admission; PACU 12 h: 12 h after PACU admission. *P=0.008; §P=0.044

Intraoperative Data

Mean PaO_2/FiO_2 values were higher in the trained group at T1 and T2, though differences did not reach statistical

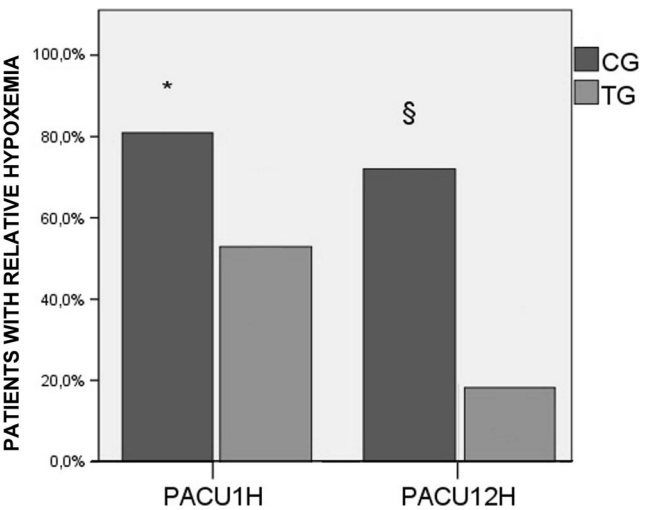

Fig. 2 Percentage of patients showing relative hypoxemia (PaO_2/FiO_2 less than 300) in the postoperative period. (PACU 1 h: 1 h after PACU admission; PACU 12 h: 12 h after PACU admission. *P=0.06; §P=0.006

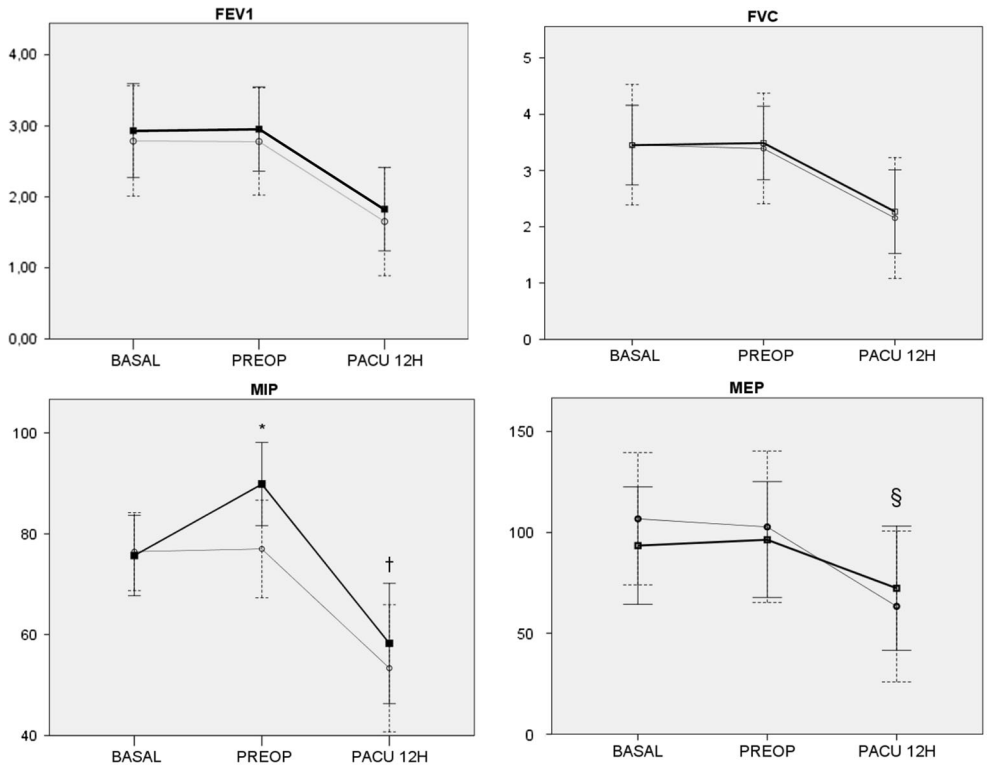

Fig. 3 Mean values of the spirometric and muscular strength parameters throughout the perioperative period. *CG* thin line, *TG* bold line. *FVC* forced vital capacity (L), *FEV-1* forced expiratory volume in 1 s (L sec^{-1}), *MIP* maximal inspiratory pressure (cm H_2O), *MEP* maximal expiratory pressure (cm H_2O). *Asterisk* between-groups statistical significance, $P<0.05$; *dagger* and *section sign* statistical significance ($P<0.01$ and $P<0.001$), respectively, for intragroup comparisons between preoperative and PACU 12 h time points, in the trained group

significance (Table 2). Mean $PaCO_2$, Csr, and EELV values did not show differences between groups at any time point. For each group of patients, PaO_2/FiO_2 and $PaCO_2$ were significantly higher at the end of surgery than after tracheal intubation (Table 2). We only recorded one postoperative complication. It was a suture dehiscence which forced a new surgery on the seventh postoperative day. The patient was a 48-year-old man from the CG with a BMI of 48.6 kg m^{-2} at the preoperative time point. He had mean PaO_2/FiO_2 values of 146 and 306 mmHg at PACU 1 h and PACU 12 h, respectively, and had four episodes of SpO_2 less than 90 % throughout his PACU stay.

Table 2 Intraoperative data

	Time point	Control group	Trained group	*P*
PaO_2/FiO_2	T1	289.5±117.5	361.0±135.8	0.70
	T2	442.6±134.9	479.6±85.8	0.29
	P	<0.00*	0.002	
$PaCO_2$ (mmHg)	T1	36.7±5.0	35.0±4.6	0.25
	T2	42.4±4.9	40.4±4.2	0.15
	P	<0.00*	<0.00*	
Csr (ml cm H_2O^{-1})	T1	50.8±11.3	51.3±9.1	0.68
	T2	58.9±13.1	61.1±12.4	0.56
	P	0.002	<0.00*	
EELV (ml)	T1	1760.4±665.6	1754.8±370.9	0.97
	T2	1865.2±465.5	1935.5±509.3	0.64
	P	0.278	0.036	

T1 after tracheal intubation, *T2* after pneumoperitoneum withdrawal, *Csr* static compliance of the respiratory system, *EELV* end-expiratory lung volume. All values are given as mean±standard deviation. *$P<0.0001$

Discussion

Our main finding was that IMT significantly improved oxygenation in the postoperative period. In the CG, 57 % of the patients showed PaO_2/FiO_2 values less than 300 at the time of PACU discharge. This means that, without supplementary oxygen, these patients would have had PaO_2 less than 60 mmHg by the time they arrived to the ward. However, in the TG, only 17 % of the patients showed relative hypoxemia at tis time point. Additionally, the MIP increased by 18.7 % in the TG during the training period and was significantly higher than in the CG at the preoperative time point. These results agree with previous studies on non-obese patients who found significant improvements in respiratory-muscle strength and endurance after preoperative physical therapy [11] [12] [13]. These studies also showed a reduction in the incidence of PPCs and in the duration of postoperative hospitalization, in patients with high [15] or low risk of PPCs [14]. In a trial aimed to study the effects of preoperative IMT on the incidence of PPCs after abdominal

surgery, Fagevik Olsen et al. [7] found that in the subgroup of obese patients, the rate for this complication decreased by sevenfold. Unlike the abovementioned studies, there were no cases of PPC in our patients. A number of reasons can explain this difference. First, our study was underpowered to determine the incidence of PPC; second, the laparoscopic approach causes less impairment on the respiratory muscular function than laparotomy or thoracotomy. Third, we carefully defined our exclusion criteria to prevent the influence of factors other than IMT on the postoperative oxygenation and so there were no risk factors for PPC in our patients other than obesity itself. In addition, the intraoperative mechanical ventilation strategy was designed to prevent pulmonary atelectasis, and so may have further affected the postoperative respiratory function. The effect of preoperative IMT on postoperative oxygenation have not been previously studied (with the exception of the study by Fagevik Olsen abovementioned [7], that shown a significant difference on oxygen saturation in favor of the treatment group on the first 3 days of the postoperative period), thus our data on this parameter cannot be directly compared with those from other studies. However, it seems reasonable to assume that the improvements in respiratory muscular function observed in trained patients could improve the lung expansion capacity during the spontaneous ventilation after surgery, improving de ventilation–perfusion mismatch, mitigating the rapid shallow breathing pattern, and thereby reducing the WOB and VO_2 usually increased in the postoperative period of the morbidly obese patients [21]. Moreover, some studies have proved that preoperative IMT leads to a decreased incidence of postoperative atelectasis [12], which, in turn, are in the basis of the ventilation/perfusion mismatch usually associated to postoperative hypoxemia.

Limitations

At the preoperative time point, BMI in the CG was 10 % higher than in the TG. This may be a major limitation because BMI seems to be directly correlated with the effects of obesity on respiratory mechanics and pulmonary gas exchange. The post hoc analysis showed that there were no correlation between BMI and PaO_2/FiO_2 in any of the two groups of patient. Thus, in this study, the expected negative influence of the increasing BMI on oxygenation did not reach statistic significance. However, a subsequent study with a larger sample would be needed in order to validate these findings.

In conclusion, we found that preventive preoperative respiratory physical therapy is associated with an improvement in postoperative oxygenation and increased inspiratory muscular strength when used in morbidly obese patients undergoing laparoscopic bariatric surgery. These results strongly warrant new studies to investigate the effects of this intervention on clinical outcomes and their cost-effectiveness.

Conflict of Interest None of the authors participating in this study have a conflict of interest to declare.

Statement of Informed Consent Informed consent was obtained from all individual participants.

Statement of Human and Animal Rights All the procedures followed in this study were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2000.

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