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Impact of an ultraviolet air sterilizer on cardiac surgery patients, a randomized clinical trial☆

María Heredia-Rodríguez[a,b], Elisa Álvarez-Fuente[a,b], Juan Bustamante-Munguira[c], Rodrigo Poves-Alvarez[a,b,*], Inmaculada Fierro[d], Esther Gómez-Sánchez[a,b], Estefanía Gómez-Pesquera[a,b], Mario Lorenzo-López[a,b], José María Eiros[f], Francisco Javier Álvarez[e], Eduardo Tamayo[e,b]

[a] Department of Anaesthesiology, Hospital Clínico Universitario, Valladolid, Spain
[b] BioCritic, Group for Biomedical Research in Critical Care Medicine, Valladolid, Spain
[c] Department of Cardiovascular Surgery, Hospital Universitario de La Princesa, Madrid, Spain
[d] Department of Health Sciences, European University Miguel de Cervantes, Valladolid, Spain
[e] Department of Pharmacology, University of Valladolid, Valladolid, Spain
[f] Department of Microbiology, Hospital Río Hortega, Valladolid, Spain

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ABSTRACT

Background: Numerous studies have evaluated the use of ultraviolet-C devices for terminal disinfection in hospitals, however, to date there is little information about the device's final impact on patients. We investigated the effect of an ultraviolet air sterilizer (UVAS) on the clinical outcomes of cardiac surgery patients.

Materials and methods: This random, prospective and non-interventional study included 1097 adult patients undergoing elective cardiac surgery: 522 stayed in an ICU room with UVAS (Medixair®) and 575 patients ICU room without UVAS and were used as a control. The primary outcome measure was to evaluate the effect of a UVAS on the overall prevalence of nosocomial infections in postoperative cardiac patients in ICUs.

Results: No significant differences in ventilator-associated pneumonia (4.6% vs. 5.0%, $p = 0.77$) and total infection (14.0% vs. 15.5%, $p = 0.45$) rates were detected in patients with and without the UVAS. The length of stay in the intensive care unit and at the hospital was similar in both groups, UVAS (4.6 (8.2) days and 18.3 (5.5) days) and without UVAS (4.6 (7.3) days and 19.2 (18.6) days). The 30-day in-hospital mortality rate was 5.3%, no significant differences between groups were observed ($p = 0.053$).

Conclusion: Novel ultraviolet-C technology has not been shown to significantly reduce nosocomial infections or mortality rates in cardiac surgery patients.

☆ Clinical trial identifier NCT02492919 (https://clinicaltrials.gov/ct2/show/NCT02492919?term=NCT02492919).

* Corresponding author.
E-mail address: rpoves@saludcastillayleon.es (R. Poves-Alvarez).

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Impacto de un esterilizador ultravioleta en pacientes de cirugía cardíaca: ensayo clínico aleatorizado

R E S U M E N

Introducción: Numerosos estudios han evaluado el uso de dispositivos ultravioleta C para la desinfección terminal en hospitales; sin embargo, hasta la fecha existen pocos datos sobre el impacto en los pacientes. Hemos evaluado el efecto de un esterilizador de aire ultravioleta (UVAS) sobre las variables clínicas de los pacientes operados de cirugía cardíaca.
Materiales y métodos: Este estudio prospectivo, aleatorizado no intervencional incluyó 1.097 pacientes adultos intervenidos de cirugía cardíaca electiva: 522 ingresaron en una habitación de UCI con UVAS (Medixair®) y 575 pacientes en habitación de UCI sin UVAS se utilizaron como control. La variable principal medida fue el efecto del UVAS sobre la prevalencia global de infecciones en el postoperatorio de cirugía cardíaca en UCI.
Resultados: No hubo diferencias significativas en la neumonía asociada a ventilación mecánica (4,6% vs. 5,0%, p = 0,77) e índices totales de infección (14,0% vs. 15,5%, p = 0,45) detectados en pacientes con y sin UVAS. La duración del ingreso en UCI y en el hospital fue similar en ambos grupos, UVAS (4,6 [8,2] días y 18,3 [5,5] días) y sin UVAS (4,6 [7,3] días y 19,2 [18,6] días). La mortalidad a 30 días hospitalaria fue del 5,3%, sin diferencias significativas entre los grupos (p = 0,053).
Conclusión La nueva tecnología ultravioleta C no ha demostrado disminuir las infecciones nosocomiales ni la mortalidad en pacientes de cirugía cardíaca.

Introduction

The environment plays an important role in the transmission of pathogens by acting as a reservoir of many multidrug-resistant bacteria, and thus, it has become an important risk factor.[1] Unfortunately, several studies have demonstrated that standard cleaning methods are currently ineffective.[2,3] Novel disinfection technologies based on hydrogen peroxide vapour, ozone mists, ultra-microfiber cloths (with copper biocide) or ultraviolet irradiation have emerged to try to resolve this problem.[4] The effectiveness of ultraviolet-C (UV-C) radiation in killing bacteria, viruses, and persistent spores has been well documented and is based on inducing the inactivation of RNA/DNA fragments via the absorption of photons, resulting in the formation of pyrimidine dimers from thymine and cytosine.[5,6]

Nosocomial infections cause considerable morbidity and mortality and represent the most common postoperative complications in an intensive care unit (ICU).[7] Pathogens involved in these infections are transmitted by direct person-to-person contact, with the skin, clothes, or when handling instruments and medical devices (catheters, intravenous lines) and through the air (respiration of particles, contamination of surgical wounds).[8] Ventilator-associated pneumonia (VAP) is one of the most common hospital-acquired infections associated with high mortality, affecting 9–27% of all intubated patients.[9] It is developed when opportunistic bacterial pathogens, such as *Pseudomonas* spp., *Acinetobacter* spp., *Enterobacteriaceae*, *Streptococci* spp., *Haemophilus* spp., and methicillin-resistant strains of *Staphylococcus aureus*, reach the pulmonary system of a patient under mechanical ventilation.[9,10] VAP is associated with a longer hospital stay, higher mortality rates, and increased healthcare costs.[11]

Medixair® (Pathogen Solutions Ltd., West Midlands, UK) is a novel and innovative portable ultraviolet air sterilizer (UVAS) that is specifically designed to decontaminate critical care environments.[12] Despite the existence of a number of studies evaluating the use of UV-C devices for terminal disinfection in hospital and ICU rooms, to date, there is little information regarding its final impact on patients.[13-16] Thus, the objective of this study was to evaluate the effect of an UVAS on the overall prevalence of nosocomial infections in postoperative cardiac patients in ICUs.

Material and methods

Setting, study design and patient inclusion

This prospective, comparative, randomized, and non-interventional study was carried out between January 2011 and January 2016 and involved patients recovering in the ICU after cardiac surgery in a third level Universitary Hospital in Spain (Clinical trial identifier #NCT02492919). Eligibility criteria to participate in the study included the following: older than 18 years, having undergone cardiac surgery (with extracorporeal circulation), having been admitted to the ICU, and signing the informed consent. The Hospital Clínico Universitario of Valladolid has 10 individual and independent rooms in the cardiac ICU. The UVAS was placed in 5 of the rooms, while the remaining rooms, which were identical to the others but did not have the UVAS, were used as a control for comparative purposes. Consecutive patients admitted into the ICU were randomly placed into each of the ICU rooms. Boxes were assigned randomly by a computer, considering those which were free that day. The primary endpoint measured was nosocomial infections rate in patients in the ICU after cardiac surgery. Secondary endpoints included length hospital stay, and determination of 30-day mortality. Other variables examined were the characterization of pathogens isolated from different sites, such as the lungs, urine, blood, surgical site (catheter), areas of the skin other than the surgical site, colonized areas (axilla, rectum, or pharynx) and other sites.

Techniques and treatment received

The surgical and anesthetic techniques and the treatment the patient received in the ICU did not differ from ordinary procedures. Antibiotic prophylaxis was performed with 2 g of cefazolin intravenously between 20 and 30 min after the induction of anesthesia, followed by 1 g every 8 h. For all interventions lasting more than 3 h, a new dose of 1 g of cefazolin was administered. Both groups of patients received the same routine respiratory care on the ICU as per the ventilator care bundle. This included appropriate hand hygiene, changing of ventilator circuits when soiled, or at 7 days whichever was sooner, and chlorhexidine 2% oral mouthwash every 6 h while intubated. Semi-recumbent body position to maintain an

angle of 40° was verified every 4 h. No selective digestive decontamination was performed. All patients routinely received gastric stress ulcer prophylaxis with Ranitidine 50 mg I.V. every 8 h. All patients were extubated in the ICU when hemodynamically stable, with a Ramsay score of 2 to 3, Tobin index (respiratory rate [spontaneous]/tidal volume [liters]) less than 105[17] pressure of arterial oxygen (PaO_2) greater than 60 mm Hg, fraction of inspired oxygen (FIO_2) less than 0.4, continuous positive airway pressure less than 5 mbar, $PaCO_2$ 50 mm Hg and arterial pH greater than 7.35. Ratio PaO_2/FIO_2 greater than 200, and there was no significant bleeding.

Ultraviolet air sterilizer

Medixair® is a portable air sterilization unit that employs the effect of ultraviolet light at 253.7 nm to achieve successful decontamination.[12] It consists of four 25-W ultraviolet low-pressure fluorescent lamps that are completely encapsulated to prevent UV leakage. The device produces a continuous airflow of 25 m^3 per hour. Microorganisms passing through the device are exposed to a minimum energy of 22,500 μW s/cm^2.[12] The working noise of the unit is less than 33 dB.

Isolation and culture of microorganisms

Samples obtained from the axilla, rectum, pharynx, nose, and groin were collected from all patients at the time of admission to the ICU and every 7 days during their hospital stay in order to determine any potential bacterial colonization. Furthermore, this study followed international guidelines, and samples obtained from lungs and blood were collected in patients with suspicion of infection prior to the start of antibiotic treatment.

Diagnosis

According to the Centers for Disease Control and Prevention, patients ventilated for >48 h were diagnosed with VAP based on the presence of new and/or progressive pulmonary infiltrates on a chest radiograph plus ≥2 of the following criteria: fever (≥38.5 °C) or hypothermia (<36 °C), leucocytosis (≥12 × 10^9/l), purulent tracheobronchial secretions, or a decrease in PaO_2/FIO_2 of at least 15% in the previous 48 h.[18] Diagnosis also included patients with a CPIS score greater than 6. Confirmation of the diagnosis included the isolation of at least one pathogenic microorganism in significant bacterial counts, i.e., ≥10^3 or 10^4 colony-forming units (CFU)/ml obtained by telescopic brushing or endotracheal aspiration, respectively. Definitions of the Centers for Disease Control and Prevention were used throughout the study, and the surveillance process was uniform for the duration of the study international guidelines for management of severe sepsis and septic shock.[18,19]

The diagnosis of septic shock was established according to the criteria provided by the international guidelines.

Surgical site infection was defined according to the Centers for Disease Control and Prevention (CDC).[20] Nosocomial urinary tract infection was verified by positive urine culture (>10^4 colony-forming units/ml of no more than two different species) obtained at least 48 h after hospital admission.

Intravenous-catheter-related bloodstream infection: isolation of the same micro-organism (i.e. identical species and antibiogram) from a semi-quantitive or quantitative culture of a catheter segment and from the blood (preferably drawn from a peripheral vein) of a patient with accompanying clinical symptoms of sepsis and no other apparent source of infection.[18]

Acute renal failure was defined as a creatinine level higher than 2 mg/dl (176.8 μmol/l) or a 50% increase in creatinine level compared with baseline.[19]

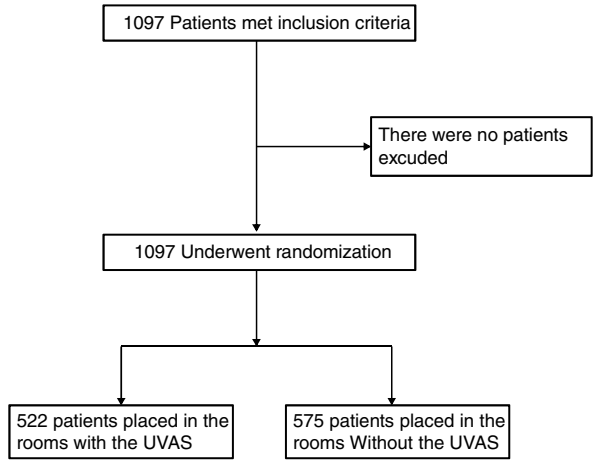

Fig. 1. Enrollment and outcomes.

Patient evaluation

During the hospitalization of the patients the responsible physician examined and treated daily. In all cases the diagnosis of infection was established by the physician responsible for the patient and confirmed by another. Physicians responsible for the study followed the patient until discharge from hospital.

Ethics issues

This study was performed according to ethics regulations and the Declaration of Helsinki. Written informed consent was sought from each patient who was asked to participate. Ethical approval for this study (Ethical Committee N° NAC 07) was provided by the Ethical Committee NAC of Hospital Clínico Universitario of Valladolid, Valladolid, Spain (Chairperson Prof FJ Bermejo-Martin) on 17 January 2011. The Medixair® manufacturer provided the devices without charge and without any conditions.

Estimation of the sample size and statistical analysis

Considering a unilateral contrast (decrease in infections when using UVAS) and starting from a global infection rate of 16% in cardiac surgery (although very variable)[21] and aiming for a reduction of infections of up to 10%, the simple size that would be needed considering a 95% CI and a statistical power of 80% is 388 patients per

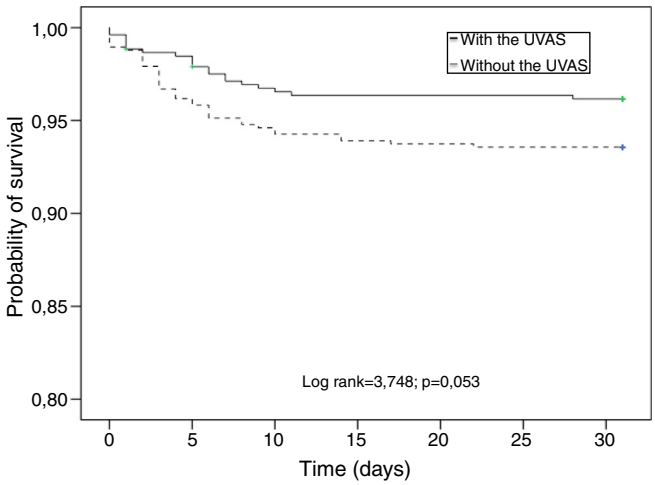

Fig. 2. Kaplan–Meier survival analysis.

Table 1
Characteristics of the patients at baseline.

	With UVAS (n = 522)	Without UVAS (n = 575)
Age. Mean years (SD)	68.6 (10.9)	67.9 (11.1)
Sex male	357 (68.4)	385 (66.9)
Weight. Mean kg (SD)	72.7 (13.3)	74.3 (16.1)
Height. Mean cm (SD)	163.4 (9.7)	164.1 (10.1)
Smoking habits	104 (19.9)	115 (20.0)
Comorbidities		
Hypertension	268 (51.3)	285 (46.6)
Diabetes mellitus	115 (22.0)	119 (20.7)
Respiratory disease	48 (9.2)	40 (6.9)
Stroke	22 (4.2)	19 (3.3)
Asthma	17 (3.3)	16 (2.8)
Endocarditis	9 (1.7)	12 (2.1)
Malignant neoplasm	2 (0.4)	7 (1.2)
Hepatic disease	2 (0.4)	4 (0.7)
Chronic renal failure	22 (4.2)	25 (4.3)
Cardiac surgery		
Emergency surgery	38 (7.3)	50 (8.7)
Perioperative parameters		
EuroSCORE I. Mean points (SD)	6.90 (6.1)	7.02 (3.8)
Type of surgery		
Valve	283 (54.2)	290 (50.4)
CABG	140 (26.8)	152 (26.4)
Valve + CABG	87 (16.7)	114 (29.8)
Other	12 (2.3)	19 (3.3)
Total CPB time. Mean min (SD)	114.4 (41.3)	117.2 (51.1)
Aortic cross-clamp time. Mean min (SD)	82.5 (33.8)	85.6 (39.03)
Postoperative parameters		
SOFA points. Mean (SD)	5.6 (1.5)	5.9 (1.9)
APACHE II points. Mean (SD)	13.5 (4.3)	13.7 (5.3)
Total duration of mechanical ventilation. Mean days (SD)	1.2 (4.8)	1.6 (5.6)
Septic shock	19 (3.6)	24 (4.17)
Reintervention for bleeding	27 (5.17)	34 (5.91)
Acute renal failure	67 (12.8)	72 (12.5)
Cardiac complications	55 (10.5)	59 (10.3)
Used antibiotics after surgery	79 (15.1)	83 (14.4)

ICU, intensive care unit; UVAS, UV air sterilizer; CABG, coronary artery bypass graft; SD, standard deviation; CPB, cardiopulmonary bypass; EuroSCORE I, European System for Cardiac Operative Risk Evaluation; SOFA, Sepsis-Related Organ Failure Assessment; SSI, surgical site infection, superficial and deep incisional.
All parameters given as *n* (%) unless otherwise stated.

group. We increased the simple by 10% to avoid the possible loss of patients and the variability of the data of infections in cardiac surgery.

Categorical variables were expressed as absolute and relative (%) frequencies, and continuous variables were expressed as the mean and standard deviation (SD). Differences between groups (with and without the UVAS) were compared using the *t*-test with continuous variables and using the chi-square test or Fisher's exact test with categorical variables. Statistical significance was established as $p \leq 0.05$. All statistical procedures were performed using SPSS 21.0 software.

Results

From a total of 1097 patients included in the study, 522 and 575 patients stayed in an ICU room with and without the UVAS, respectively (Fig. 1). The patients were predominantly male (67.6% of the total), with a mean age of 68.3 (11.1) years, and had no smoking habits (80.0%). The most common comorbidities in patients were hypertension (50.4% of the total) and diabetes (21.3%). A total of 8.0% of patients underwent emergency cardiac surgery. EuroSCORE I was similar between the groups, with 6.90 (6.1) points in patients with the UVAS and 7.02 (3.8) points in patients without the UVAS (Table 1).

Table 2
Analytical results at the time of admission to the ICU (1) and maximum peaks reached (2) in patients placed in the rooms with the UVAS and the control group without the UVAS.

Parameters	With UVAS (n = 522)	Without UVAS (n = 575)
1-Troponin T (μg/l)	842.9 (1605.6)	880.6 (1276.4)
2-Troponin T (μg/l)	945.2 (1529.8)	1074.0 (2534.3)
1-CPK (ng/ml)	711.0 (2881.2)	619.9 (1051.5)
2-CPK (ng/ml)	1036.0 (1436.5)	1042.7 (1936.9)
1-CK-MB (ng/ml)	55.1 (62.1)	58.7 (89.8)
2-CK-MB (ng/ml)	47.2 (49.6)	52.6 (103.9)
1-GOT (ng/ml)	78.5 (159.8)	74.4 (227.5)
2-GOT(ng/ml)	96.5 (282.4)	137.1 (696.7)
1-LDH (ng/ml)	369.7 (205.4)	384.7 (447.4)
2-LDH (ng/ml)	392.0 (252.4)	443.4 (769.3)
1-Hemoglobin (g/dl)	10.2 (1.5)	9.9 (1.4)
1-Haematocrit (%)	30.6 (4.3)	30.1 (4.1)
1-Leukocytes (×103/μl)	11.3 (4.5)	11.1 (4.1)
1-Monocytes (×103/μl)	5.3 (2.6)	5.6 (2.5)
1-Neutrophils (%)	83.1 (6.4)	83.0 (5.6)
1-Mg, mmol/l	1.6 (0.2)	1.6 (0.3)
1-Na, mmol/l	140.4 (3.2)	140.3 (3.1)
1-K, mmol/l	4.0 (0.6)	4.0 (0.6)
1-Glucose (mg/dl)	104.8 (3.7)	105.1 (3.4)
1-Urea (mg/dl)	44.3 (20.0)	44.6 (16.6)
1-Creatinine (mg/dl)	1.0 (0.4)	1.1 (0.6)
1-Bilirubin (mg/dl)	0.9 (0.7)	0.9 (0.6)
1-Glucose (mg/dl)	176.3 (45.6)	181.3 (55.2)
1-CRP (mg/l)	13.0 (23.3)	14.8 (26.1)
1-Procalcitonin (ng/ml)	0.4 (1.0)	0.2 (0.3)

Values are expressed as means (SD).
CPK, creatine phosphokinase; CK-MB, creatine kinase-MB; GOT, aspartate aminotransferase; Mg, magnesium; Na, sodium; K, potassium; LDH, lactate dehydrogenase; CRP, C-reactive protein.

The postoperative course into the groups showed no significant differences in levels of troponin, hemoglobin, haematocrit, leukocytes, ions, glucose, urea, creatinine, bilirubin and CRP. Analytical results at the time of admission to the ICU and maximum peaks reached in our patients are detail in Table 2 and, with exception of procalcitonin, no significant differences were observed between groups with and without UVAS. There were no significant differences in bacterial colonization from samples of patients with and without the UVAS, considering any type of bacteria (40.4% and 43.1%, respectively), Gram-positive (21.6% and 24.3%, respectively) or Gram-negative (18.8% in both groups); these results are shown in Table 3. In addition, no differences were observed when different locations were taken into account. The description of the microorganisms isolated from different sites on patients is shown in Table 3.

One hundred twenty-five (11.4%) patients acquired nosocomial infections during their hospital stay (1.29 nosocomial infections per infected patient). Eighty-eight (70.4%) patients developed a single infection and 37 (29.6%) patients had multiple nosocomial infections. 58 patients with UVAS (11.1%) and 67 patients without UVAS (11.1%) were infected, without significant differences (p = 0.919, OR = 1.018, 95% CI: 0.720–1.440). VAP was the most frequent infection. Although not statistically significant (p = 0.77), the frequency of developing VAP was slightly lower in patients with the UVAS (4.6%) than in patients without UVAS (5.0%). No significant differences were observed in urinary tract, catheter, blood and surgical site infection (Table 4). The length of stay in the ICU and at the hospital was similar in patients with the UVAS (4.6 (8.2) days and 18.3 (5.5) days) compared with patients without UVAS (4.6 (7.3) days and 19.2 (18.6) days). The 30-day in-hospital mortality rate was 5.3%. No significant differences were detected in patients with (3.8%) and without (6.4%) the ultraviolet air sterilizer (p = 0.053, OR = 0.679, 95% CI: 0.393–1.173). Kaplan–Meier survival

Table 3
Description of microorganisms isolated from different sites of infection in patients placed in rooms with the ultraviolet air sterilizer (UVAS) ($n = 575$) and the control group without the UVAS ($n = 522$).

	Lungs		Urine		Catheter		Blood		Area of skin other than surgical site		Colonized areas (axilla, rectum, pharynx)	
	Without UVAS	With UVAS	Without UVAS	With UVAS	Without UVAS	With UVAS	Without UVAS	With UVAS	Without UVAS	With UVAS	Without UVAS	With UVAS
Gram-positive cocci	12	4	3	4	14	10	34	29	59	51	18	15
Staphylococcus aureus	8	4	0	0	0	2	5	7	7	10	18	14
Methicillin resistance S. aureus	0	0	0	0	0	0	1	0	0	0	0	0
Staphylococcus epidermidis	1	0	0	0	9	7	14	12	25	26	0	0
Other Staphylococcus spp.	0	0	0	0	2	1	7	7	6	2	0	1
Streptococcus pneumoniae	2	0	0	0	0	0	0	0	0	0	0	0
Other Streptococcus spp.	0	0	0	0	1	0	1	0	3	2	0	0
Enterococcus faecalis	0	0	0	1	1	0	3	0	3	2	0	0
Enterococcus faecium	1	0	2	1	0	0	1	2	0	0	0	0
Other Gram-positive cocci	0	0	0	2	1	0	2	1	10	8	0	1
Gram-negative bacilli	20	20	18	18	8	10	13	11	19	17	30	22
Escherichia coli	3	0	5	6	1	1	1	1	7	3	4	5
Klebsiella spp.	6	4	5	5	1	0	6	4	4	4	16	7
Enterobacter spp.	0	1	3	1	2	3	3	3	1	4	0	2
Haemophilus influenzae	6	11	0	0	0	1	0	0	0	0	1	2
Pseudomonas aeruginosa	3	2	2	3	1	1	1	0	1	0	2	1
Acinetobacter spp.	2	1	1	1	2	1	1	0	3	3	4	3
Bacteroides spp.	0	0	0	0	0	0	0	0	1	1	0	0
Other Gram-negative bacilli	0	1	2	2	0	3	1	3	2	2	3	2
Fungi	6	6										
Candida albicans	5	4	1	4	0	1	0	1	2	0	2	7
Other C. albicans spp.	1	2	0	1	2	0	0	0	1	1	3	8

Table 4
Study outcomes.

	With UVAS (*n* = 522)	Without UVAS (*n* = 575)	Significance (*p*)
Clinical outcomes			
Site of infection			
Patients developing VAP	24 (4.6)	29 (5.0)	0.77
Urinary tract	15 (2.9)	15 (2.6)	0.78
Catheter	6 (1.4)	9 (1.6)	0.71
Blood	13 (2.4)	16 (2.8)	0.78
Surgical site infection	15 (2.8)	20 (3.5)	0.56
SSI	9 (1.7)	13 (2.3)	
Organ-space SSI	6 (1.1)	7 (1.2)	
Total infection	73 (14.0)	89 (15.5)	0.45
Preoperative hospitalization. Mean days (SD)	5.7 (7.7)	5.5 (7.8)	0.75
Stay in the ICU. Mean days (SD)	4.6 (8.2)	4.6 (7.3)	0.98
Postoperative stay. Mean days (SD)	8.6 (10.1)	9.2 (13.5)	0.42
Total stay at the hospital. Mean days (SD)	18.3 (5.5)	19.2 (18.6)	0.38
30-day mortality rate	20 (3.83)	37 (6.4)	0.053

ICU, intensive care unit; UVAS, UV air sterilizer; SD, standard deviation; SSI, surgical site infection, superficial and deep incisional.
All parameters given as n (%) unless otherwise stated.

Table 5
Demographic, clinical, and perioperative characteristics of survivor and non-survivor patients who underwent cardiac surgery and were admitted to the ICU.

Characteristics	Survivors (*n* = 1040)	Non-survivors (*n* = 57)	Significance (*p*)
Age. Mean years (SD)	68.1 (11.1)	70.3 (11.2)	0.13
Sex male. *N* (%)			
Weight. Mean kg (SD)	73.5 (4.8)	75.4 (15.4)	0.38
Height. Mean cm (SD)	163.7 (9.9)	165.1 (9.5)	0.41
Smoking habits	214 (20.5)	9 (15.70)	0.39
Comorbidities. *N* (%)			
Hypertension	528 (50.7)	27 (47.3)	0.642
Diabetes mellitus	222 (21.3)	13 (22.8)	0.77
Respiratory disease	83 (7.9)	5 (8.7)	0.82
Stroke	41 (3.9)	1 (1.7)	0.40
Asthma	31 (2.9)	2 (2.4)	0.81
Endocarditis	20 (1.9)	1 (1.7)	0.93
Malignant neoplasm	10 (0.9)	0 (0.0)	0.45
Hepatic disease	6 (0.6)	1 (1.7)	0.27
Chronic renal failure	39 (3.8)	8 (14.9)	**0.0001**
Cardiac surgery			
Emergency surgery. N (%)	75 (7.2)	15 (26.3)	**0.0001**
Perioperative parameters			
Left ventricular ejection fraction. % (SD)	55.6 (10.2)	51.7 (14.6)	**0.01**
EuroSCORE. Mean points (SD)	6.7 (4.3)	12.1 (12.1)	**0.0001**
Type of surgery. N (%)			0.47
Valve	545 (52.42)	28 (49.12)	
CABG	280 (26.90)	12 (21.05)	
Valve+CABG	186 (17.88)	15 (26.31)	
Other	28 (2.69)	3 (5.26)	
Total CPB time. Mean min (SD)	113.9 (43.1)	159.1 (84.3)	**0.0001**
Aortic cross-clamp time. Mean min (SD)	83.2 (35.5)	106.9 (55.4)	**0.0001**
Postoperative parameters			
SOFA points. Mean (SD)	5.5 (1.7)	7.7 (1.7)	**0.0001**
APACHE II points. Mean (SD)	13.3 (3.8)	18.3 (5.6)	**0.0001**
Respiratory failure. N (%)	82 (5.8)	37 (64.9)	**0.0001**
Septic shock	35 (4.13)	8 (14.0)	0.004
Reintervention for bleeding	45 (4.3%)	16 (28.0%)	**0.0001**
Acute renal failure	120 (9.0)	19 (33.3)	**0.0001**
Cardiac complications	97 (2.3)	17 (29.0)	**0.0001**
Patients who used ANTIBIOTICS postoperatively	144 (13.8)	22 (38.6)	**0.0001**
Clinical outcomes			
Site of infection			
Patients developing VAP. *n* (%)	41 (3.9)	12 (21.0)	**0.0001**
Urinary tract	26 (2.5)	4 (7.0)	0.11
Catheter	9 (0.8)	6 (10.5)	0.003
Blood	21 (2.0)	8 (14.0)	0.0001
Surgical site infection	30 (2.8)	5 (0.5)	0.063
SSI	21 (2.0)	1 (0.1)	
Organ/space SSI	9 (0.8)	4 (0.4)	
Total infection	127 (12.2)	35 (61.5)	**0.0001**

Table 5 (*Continued*)

Characteristics	Survivors (n = 1040)	Non-survivors (n = 57)	Significance (p)
Preoperative hospitalization. Mean days (SD)	5.7 (7.8)	4.1 (5.7)	0.14
Stay in the ICU. Mean days (SD)	4.6 (7.9)	4.4 (4.1)	0.83
Postoperative stay. Mean days (SD)	9.4 (12.1)	0.9 (3.5)	**0.0001**
Total stay at the hospital. Mean days (SD)	19.3 (17.4)	9.2 (8.9)	**0.0001**

ICU, intensive care unit; UVAS, UV air sterilizer; CABG, coronary artery bypass graft; SD, standard deviation; CPB, cardiopulmonary bypass; EuroSCORE, European System for Cardiac Operative Risk Evaluation; SOFA, Sepsis-Related Organ Failure Assessment; SSI, surgical site infection, superficial and deep incisional.
All parameters given as *n* (%) unless otherwise stated.

Table 6
Analytical results at the time of admission to the ICU (1) and maximum peaks reached (2) in survivor and non-survivor patients.

Parameters	Survivors (n = 1040)	Non-survivors (n = 57)	p value
1-Troponin T (μg/l)	806.1 (1282.8)	2247.9 (3487.1)	0.0001
2-Troponin T (μg/l)	884.9 (1445.3)	3831.2 (7061.1)	0.0001
1-CPK	659.6 (2214.8)	826.3 (854.8)	0.702
2-CPK	1009.8 (1651.3)	1712.7 (2568.1)	0.041
1-CK-MB (ng/ml)	54.6 (75.2)	112.9 (109.8)	0.033
2-CK-MB (ng/ml)	46.1 (70.0)	129.6 (188.5)	0.0001
1-GOT	65.1 (100.1)	358.9 (832.2)	0.0001
2-GOT	84.2 (251.8)	853.6 (2206.5)	0.0001
1-Hemoglobin	10.1 (1.4)	9.5 (1.8)	0.100
1-Haematocrit (%)	30.4 (4.2)	28.8 (5.2)	0.164
1-Leukocytes ($\times 10^3$/μl)	11.1 (4.2)	12.8 (6.7)	0.007
1-Monocytes ($\times 10^3$/μl)	5.4 (2.5)	5.9 (2.5)	0.598
1-Neutrophils (%)	83.1 (6.0)	83.0 (6.5)	0.517
1-Platelets ($\times 10^3$/μl)	137.0 (53.1)	104.8 (44.0)	0.704
1-Mg	1.6 (0.3)	1.7 (0.2)	0.542
1-Na (mmol/l)	140.4 (3.1)	140.8 (4.8)	0.008
1-K (mmol/l)	4.0 (0.6)	4.4 (0.7)	0.130
1-Glucose (mg/dl)	105.0 (3.5)	104.4 (3.8)	0.465
1-Urea (mg/dl)	44.2 (18.1)	50.9 (23.8)	0.502
1-Creatinine (mg/dl)	1.0 (0.5)	1.3 (0.6)	0.020
1-Bilirubin (mg/dl)	0.9 (0.6)	1.3 (0.9)	0.006
Glucose (mg/dl)	177.6 (48.8)	206.9 (79.1)	0.0001
1-LDHu	358.1 (182.0)	847.0 (1462.7)	0.0001
2-LDHu	377.4 (278.5)	1327.7 (2309.6)	0.0001
1-CRP (mg/l)	13.4 (24.0)	27.4 (35.6)	0.002
1-Procalcitonin (ng/ml)	0.3 (0.8)	0.3 (0.5)	0.960
1-Lactate (mg/dl)	0.3 (0.2)	0.6 (0.6)	0.0001

Values are expressed as the mean (SD).
CPK, creatine phosphokinase; CK-MB, creatine kinase-MB; GOT, aspartate aminotransferase; Mg, magnesium; Na, sodium; K, potassium; LDH, lactate dehydrogenase; CRP, C-reactive protein.

analysis revealed that the percentage of survival was not different between patients with and without UVAS (Log rank = 3.748; p = 0.053; Fig. 2).

Discussion

To the best of our knowledge, the effect of UV-C devices on the clinical outcomes of cardiac surgery patients in an ICU has not been previously reported. Characteristics of both groups are summarized in Table 1 demonstrating general similarities. This study demonstrated that the use of Medixair® did not provide clinical benefits associated with a reduced incidence of nosocomial infections in postoperative cardiac patients in the ICU. In addition, there were no differences in the number of infections, VAP, renal or surgical site infections, or bacteraemia cases between the group with the UVAS and the control group. There were no differences in the length of stay in the hospital or length of stay in the ICU and 30-day mortality between the group with the UVAS and the control group (Tables 5 and 6).

An endotracheal tube is considered to be one of the major risk factors for VAP, (i) acting as a reservoir for opportunistic pathogen bacteria by allowing the formation of biofilms, (ii) enabling bacterial invasion by providing a direct pathway for airborne pathogens to reach the lungs, and (iii) impairing the body's natural defence (preventing the cough reflex, for instance) and mucociliary clearance. Consistent with findings obtained in pilot studies, our UVAS was shown to reduce the abundance of pathogens reaching the lungs of patients in the ICU. Despite not being clinical studies, there are a few experimental studies evaluating the effectiveness of similar UV-C devices on the decontamination of hospital rooms.[6,22–25] UV-C radiation reduced the abundance of vegetative bacteria on surfaces by 99.9% in 15 min, and 99.8% of *Clostridium difficile* spores were reduced in 50 min.[23] Overall, UV-C decreased the frequency of positive cultures of MRSA and vancomycin-resistant *Enterococcus* by approximately 93% and 80% of *C. difficile*.[24] Furthermore, to the best of our knowledge, only one clinical trial has been performed to evaluate the effect of UV irradiation on clinical and epidemiological features in patients.[25] Specifically, this trial, which involves patients from the neonatal ICU and evaluates the effect of enhanced ultraviolet germicidal irradiation installed in the heating, ventilation and air conditioning system, showed a reduction in environmental microbes, in the number of patients with tracheal colonization (from 74% to 39%), in the number of VAP episodes per patient (from 1.2% to 0.4%), as well as a decrease in the use of antibiotics (62%). As reported in the literature, the most common bacterial isolates causing VAP involve aerobic Gram-negative bacilli (58% of isolates, specifically *Pseudomonas aeruginosa* and *Enterobacteriaceae*, such as *Escherichia coli*, *Proteus* spp., *Enterobacter* spp., and *Klebsiella* spp.) and Gram-positive cocci (up to 35% of isolates, mainly *S. aureus*).[26] In our study, despite isolating fewer *S. aureus* in patients with the UVAS, the incidence of VAP was similar between both groups, indicat-

ing that the contribution of UV-C to the prevention of VAP was minimal.

Importantly, potential photokeratitis and ocular symptoms are risks that are associated with the application of UV-C. Long-term toxicity after accidental exposure has been reported.[27] Thus, appropriate measures defined in specific guidelines for human exposure to UV-C were applied. However, these measures should be optimized to avoid any decrease in germicidal efficacy.[28]

Our study presents a 30-day in-hospital mortality rate of 5.3%, which might seem high if compared to other studies carried out in Europe, such as, for example Barili et al. (3.4%, operative deaths).[29] However, this observed mortality rate is comparable to the results reported by Spanish Society of Thoracic-Cardiovascular Surgery.[30] Moreover, in our study 30-day in-hospital mortality showed no significant differences in patients with UVAS vs. without UVAS ($p = 0.053$). This finding is in accordance with no differences in the ratio of VAP between both groups were observed.

An important limitation of the study was the lack of information related to the environmental abundance of pathogens, including information in areas close to the patient. Although these data might have provided additional useful information about the reservoir of pathogens in the ICU room, we preferred to directly examine the effect of the UVAS on the pathogens that finally reached the patient. Other limitations of the study included the *Hawthorne effect*, since the study was open, and the design, as it was carried out in a single center with a limited population of post-cardiac surgery patients admitted to a 10-bed cardiac intensive care unit.[7] Consequently, any conclusions can only be drawn in this context.

Conclusion

In conclusion, novel UV-C technology did not appear to provide additional benefits in reducing the incidence of nosocomial infections in cardiac surgery patients in ICU stay. Moreover, the use of the UVAS did not appear to contribute to decreasing the 30-day mortality rate observed. On the basis of these results, large prospective and randomized clinical trials are required to further characterize the effects of UV-C devices in the disinfection of intensive care facilities and to evaluate their effect on the outcomes of critical patients in the ICU.

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Author contributions

MHR, EAF and ET conceived the idea, designed the protocol, and supervised the analysis of the results. EGS, FJA. EGP and JME supervised the recruitment of patients and collected the clinical material. IF, FJA, MLL, ET, and JBM developed and supervised all work and analyzed the results. ET, EAF, JME, RPA and JBM wrote the report in collaboration with all the authors.

Conflict of interest

The authors declare no conflicts of interest.

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