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Postoperative Visual and Auditory Hallucinations after Cardiac Surgery: VAACS Umbrella Study

Haitham Abu Khadija [1], Nizar Abu Hamdeh [2,11], Duha Najajra [2,11], Wafiq Othman [5], Hamza A. Abdul-Hafez [2,11], Anwar Zahran [2,11], Omar Heih [2,6], Yahya Z. Fraitekh [2,23], Mohammad Masu'd[2,11] , Mahdi Awwad[2,11], Idiberto José Zotarelli Filho[2,12], Alaa Zayed[2,11], Moaath Sawalha [2,11] , Sara Ismail [2,11] , Izzeddin Swidan[2,11] , Omar Abu-Hamda [2,6], Oday Nana[2,11] , Qassem Hamoudy[2,11] , Basem Bali[2,11] , Moaath Nairat [7], Issa Al-Khdour [8], Ahmad Darwazah [9], Bisher Marzouqa[22], Mohammad Sbaih [13], Mustafa Shehadeh[22,] Khalil Bali[24], Hasan Alkhatib [10], Helmi Tamimi [10], Ala Rubi [25] , Nahi N. Al-aydi [26] , Ro'a Khalaf [2,14], Saja Karam[2,11], Aya Atatra [2,14], Ibraheem AbuAlrub[2,11] , Raya Fuqha[2,11] , Zahra'a Alhaj[2,11], Lila Abubilal [2,10], Wajeh Abuirmaileh [2,16], Mohammad Yasini [2,16], Alaa Dabash[2,11], Seleen Abu-Alhmam [2,16], Deema Mhesin [2,17], Saeed Bakeer[2,11] , Yazan Hamdan[2,11] , Osama Ewidat[2,11] , Motasem Zahaika[2,11] , Hanan Jboor[2,11] , Abdalkarim Ali[2,11] , Abdalfatah Badran[2,11] , Kamal Issa[2,11] , Abdelrahman Salous[2,11] , Ghina Abukamleh [2,6], Merna Hazaza [2,18], Rou'a Farah [2,6], Rahaf Farah [2,6], Husam Abuzaina[2,11] , Roua Najjar [2,6], Ameen Abu-Awad [2], Ayat Aljuba [2,6], Balqis Shawer [2,6], Omar Salah [2,19], Majd Shehadeh [2,20], Inas Jaber [2,16], Fatima Manassra [2], Doha Jaber [2,16], Batoul Jayouse [2,21], Yara Assaf [2,20], Ali Alrifai [2,20], Lourin Abuhaniah [2], Maya Altmaizee [2], Abdalaziz Darwish[2,11*], Mohammad Alnees[1,3,4,*]

Affiliations:

[1] Heart Center, Kaplan Medical Center, Pasternak St. 1 Rehovot, affiliated with the Hebrew University, Jerusalem. Israel.

[2] Palestinian Clinical Research Center, Bethlehem, Palestine.

[3]Harvard Medical School Postgraduate Medical Education, Global Clinical Scholars Research Training program, Boston, US.

[4]Head of Palestinian Clinical Research Center, Bethlehem, Palestine.

[5] Department of Anesthesia, An-Najah National University Hospital, Nablus, Palestine.

[6] Faculty of Medicine, Palestine Polytechnic University, Hebron, Palestine.

[7] Department of Cardiothoracic Surgery, An-Najah National University Hospital, Nablus, Palestine.

[8] Department of Cardiothoracic Surgery, Istishari Arab Hospital, Ramallah, Palestine.

[9] Department of Cardiothoracic Surgery, Palestine Medical Complex, Ramallah, Palestine.

[10] Department of Cardiac surgery, Al Makassed Hospital, Jerusalem, Palestine.

[11] Department of Medicine, Faculty of Medicine and Health Sciences, An-Najah National University, Nablus, Palestine.

[12] UNESP - São Paulo State University. Institute of Biosciences, Humanities and Exact Sciences (Ibilce), Postgraduate Program in Food, Nutrition and Food Engineering, Campus São José do Rio Preto, SP, CEP 15054-000, Brazil.

[13] Specialist Cardiac Surgeon, Nablus Speciality Hospital, Nablus, Palestine.

[14] Jenin Governmental Hospital, Jenin, West Bank, Palestine.

[15] Ibn-Sina Hospital, Jenin, Palestine.

[16] Faculty of Medicine, Al-Quds University, Jerusalem, Palestine

[17] Specialized Arab Hospital, Nablus, Palestine

[18] Abu Al-Hassan Al-Qasim (Yatta) hospital, Hebron, Palestine.

[19] Intern, Department of Medicine, Shamir Medical Center (Assaf Harofeh), Zerifin, Israel.

[20] Palestine Medical Complex, Ramallah, Palestine.

[21] Department of Medicine, The Arab American University, Jenin, Palestine.

[22] Alahli Hospital, Hebron, Palestine

[23] Clinical Research Program, Faculty of Graduate Studies, An-Najah National University, Nablus, Palestine.

[24] Department of Medicine, Division of Cardiac Surgery, Ibn Sina Specialized Hospital, Jenin, Palestine.

[25] Head of the Department of Cardiac Surgery, Consultant Cardiac Surgeon, Specialized Arab Hospital, Nablus, Palestine.

[26] Specialist Cardiac Surgeon, Specialized Arab Hospital, Nablus, Palestine.

(*) Mohammad Alnees (Corresponding author)
Dr Mohammad Alnees, Harvard Medical School, Postgraduate Medical Education, Global Clinical Scholars Research Training program, Boston, US.
Email: a2011z2012z2013@gmail.com
https://orcid.org/0000-0002-5577-8499
Mobile: +970599240098

(*) Abdalaziz Darwish (Corresponding author)
Dr Abdalaziz Darwish, Department of Medicine, Faculty of Medicine and Health Sciences, An-Najah National University, Nablus, Palestine.

Email: Abdalaziz.darwish1@gmail.com

https://orcid.org/0000-0002-3231-3672

Mobile: +97259-202-6839

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Affiliations:

[1] Heart Center, Kaplan Medical Center, Pasternak St. 1 Rehovot, affiliated with the Hebrew University, Jerusalem. Israel.

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[3]Harvard Medical School Postgraduate Medical Education, Global Clinical Scholars Research Training program, Boston, US.

[4]Head of Palestinian Clinical Research Center, Bethlehem, Palestine.

[5] Department of Anesthesia, An-Najah National University Hospital, Nablus, Palestine.

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[7] Department of Cardiothoracic Surgery, An-Najah National University Hospital, Nablus, Palestine.

[8] Department of Cardiothoracic Surgery, Istishari Arab Hospital, Ramallah, Palestine.

[9] Department of Cardiothoracic Surgery, Palestine Medical Complex, Ramallah, Palestine.

[10] Department of Cardiac surgery, Al Makassed Hospital, Jerusalem, Palestine.

[11] Department of Medicine, Faculty of Medicine and Health Sciences, An-Najah National University, Nablus, Palestine.

[12] UNESP - São Paulo State University. Institute of Biosciences, Humanities and Exact Sciences (Ibilce), Postgraduate Program in Food, Nutrition and Food Engineering, Campus São José do Rio Preto, SP, CEP 15054-000, Brazil.

[13] Specialist Cardiac Surgeon, Nablus Speciality Hospital, Nablus, Palestine.

[14] Jenin Governmental Hospital, Jenin, West Bank, Palestine.

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[16] Faculty of Medicine, Al-Quds University, Jerusalem, Palestine

[17] Specialized Arab Hospital, Nablus, Palestine

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[22] Alahli Hospital, Hebron, Palestine

[23] Clinical Research Program, Faculty of Graduate Studies, An-Najah National University, Nablus, Palestine.

[24] Department of Medicine, Division of Cardiac Surgery, Ibn Sina Specialized Hospital, Jenin, Palestine.

[25] Head of the Department of Cardiac Surgery, Consultant Cardiac Surgeon, Specialized Arab Hospital, Nablus, Palestine.

[26] Specialist Cardiac Surgeon, Specialized Arab Hospital, Nablus, Palestine.

(*) Mohammad Alnees (Corresponding author)
Dr Mohammad Alnees, Harvard Medical School, Postgraduate Medical Education, Global Clinical Scholars Research Training program, Boston, US.
Email: a2011z2012z2013@gmail.com
https://orcid.org/0000-0002-5577-8499
Mobile: +970599240098

(*) Abdalaziz Darwish (Corresponding author)
Dr Abdalaziz Darwish, Department of Medicine, Faculty of Medicine and Health Sciences, An-Najah National University, Nablus, Palestine.

Email: Abdalaziz.darwish1@gmail.com

https://orcid.org/0000-0002-3231-3672

Mobile: +97259-202-6839

Abstract

Background

Hallucinations are underrecognized neuropsychiatric complications after cardiac surgery. Data on incidence and type-specific predictors in coronary artery bypass grafting (CABG) and valvular surgery are limited.

Methods

We conducted a multicenter prospective cohort study (September 2022 to May 2025) across West Bank cardiac surgery centers. A total of 1,332 adults (997 CABG, 335 valve) were assessed daily for 7 days postoperatively using the Questionnaire for Psychotic Experiences. Predictors of visual and auditory hallucinations evaluated with Cox proportional hazards models.

Results

Visual hallucinations occurred in 11.5% of CABG patients and 10.0% of valve surgery patients, while auditory hallucinations were reported in 7.0% and 5.0%, respectively. In the CABG group, the multivariable Cox regression models stratified by hospital showed that auditory hallucinations were significantly associated with lower left ventricular ejection fraction (HR = 1.05 per 1% decrease; 95% CI 1.01–1.09), longer aortic cross-clamp time (HR = 1.01 per minute; 95% CI1.0004–1.02), and immunosuppressive therapy (HR = 4.81; 95% CI 1.13–20.53). Postoperative blood transfusion was associated with an increased risk of visual hallucinations in univariate analysis (HR = 1.87; 95% CI 1.05–3.33), but the association became borderline after adjustment (HR = 1.97; 95% CI 0.95–4.09). Among the valve surgery cohort, the hospital-stratified models indicated that prolonged postoperative ventilation was independently protective against visual hallucinations (adjusted HR = 0.78; 95% CI 0.68–0.90), whereas noradrenalin use (adjusted HR = 6.07; 95% CI 2.18–16.93) and immunosuppressive therapy (adjusted HR = 5.13; 95% CI 1.14–23.09) markedly increased the risk. For auditory hallucinations in valve surgery patients, adrenaline exposure emerged as a significant independent predictor (adjusted HR = 3.40; 95% CI 1.21–9.54.

Conclusions

Postoperative hallucinations affected ~1 in 10 patients; visual hallucinations were more frequent, auditory hallucinations linked to stress and medications, with risks varying by surgery type, supporting tailored monitoring and prevention.

Keywords: cardiac surgery, CABG, valve replacement, postoperative hallucinations, visual hallucinations, auditory hallucinations, Cox regression, risk stratification, critical care, vasopressors, immunosuppression, mechanical ventilation

Introduction:

During the 20th century, cardiopulmonary bypass (CPB) revolutionized cardiovascular surgery by temporarily replacing heart and lung function, enabling transformative open-heart procedures (1). Each year, more than 400,000 coronary artery bypass graft (CABG) surgeries are performed in the United States, using vessel grafts to bypass coronary occlusions and restore blood flow, either on-pump with CPB or off-pump on a beating heart (2)(3). Surgical complications include stroke, wound infection, graft failure, postoperative atrial fibrillation, and rarely, mortality (1–2%) (3)(4). Heart valve replacement or repair is the second most common cardiac procedure, with over 1 million operations from 1993 to 2007 (5)(6). These procedures replace damaged valves with mechanical or biological prostheses, differing in longevity and anticoagulation needs (7). Postoperative complications may include arrhythmias, heart failure, and valve dysfunction (8)(9).

Auditory and visual hallucinations, often vivid, colorful, and involving people or objects, are increasingly recognized after major surgery (10)(11). While often linked to delirium, they can occur independently as a distinct neurocognitive complication (10). After cardiac procedures like CABG or valve surgery, hallucinations are typically visual, transient, and non-distressing (12)(13)(14), with a prevalence of around 21% in prior studies (15)(16). Proposed mechanisms include disrupted brain connectivity, cholinergic deficits, inflammation, medications, and cerebral changes from cardiopulmonary bypass (12)(17) (18). Perioperative hallucinations are often underrecognized or misattributed to delirium. The Questionnaire for Psychotic Experiences (QPE) systematically assesses auditory, visual, tactile, olfactory, sensed presence, and delusional experiences in surgical patients (12)(19).

Postoperative hallucinations can impair recovery by causing distress, anxiety, self-removal of devices, self-harm, and reduced treatment adherence (15)(20). These effects may delay rehabilitation, prolong ICU stays, and increase serious complications (15)(20). Literature often groups hallucinations with broader psychiatric or cognitive complications, without defining their frequency, risk factors, or features, especially in CABG versus valve surgery patients. This multicenter prospective cohort study aims to fill this gap by comparing hallucination incidence and clinical features between these two groups.

Methods

Study design, setting, and population

We conducted a multicenter prospective cohort study of postoperative hallucinations in cardiac surgery patients over 3 years (September 2022 through May 2025) at all major cardiac surgery centers in the West Bank, Palestine. These included Ibn Sina Specialist Hospital, Specialized Arab Hospital, An-Najah National University Hospital, Al-Razi Hospital, Al-Mezan Hospital, Al-Ahli Hospital, Arab Society for Rehabilitation, Palestine Medical Complex, Nablus Specialty Hospital, and Al-Makassed Hospital, representing the region’s cardiac surgical critical care units (CCUs).

Because the study aimed to directly compare postoperative hallucinations between isolated CABG and isolated valve surgery, patients who underwent concomitant CABG and valve procedures were excluded. These combined operations involve longer cardiopulmonary bypass and cross-clamp times, higher perioperative risk, and distinct hemodynamic and pharmacologic profiles, which could confound group-specific associations.

Setting and timeline:

This prospective multicenter cohort was conducted within the VAACS program across all major cardiac surgery centers in the West Bank. Recruitment occurred from September 2022 to May 2025. Hallucination outcomes were assessed prospectively during the first 7 postoperative days (daily bedside QPE on POD1–4 with surveillance to day 7). No patient-level follow-up beyond day 7 was included in this analysis.

Study Population and Data Collection

Adult patients (≥18 years) undergoing elective or semi-elective isolated CABG or valve surgery were prospectively enrolled in the VAACS multicenter study. Key exclusions included severe neuropsychiatric or sensory disorders, active substance abuse, or emergency surgery. Consecutive eligible patients were stratified (CABG vs. valve) and followed from admission through the early postoperative period. Standard institutional perioperative protocols were used across centers. Comprehensive demographic, clinical, laboratory, and intra-/postoperative variables were extracted from medical records, including EuroSCORE II and detailed medication use. Patients with perioperative or postoperative shock were excluded from the study because they were not eligible for postoperative psychiatric evaluation due to sedation, mechanical ventilation, or unstable clinical status. All included participants were hemodynamically stable, extubated, and oriented at the time of interview.

To account for intraoperative hemodynamic stability, the variable "hemostasis at closure" was included as a practical surrogate measure reflecting intraoperative blood loss control, coagulatory adequacy, and overall operative stability. This variable has been previously described as an indicator of surgical field control and tissue perfusion balance in cardiac surgery. **See eAppendix 1. in Supplementary File 1 for full eligibility criteria, surgical methods, and variable definitions [23–25].**

Surgical Procedures

Operative data were collected from intraoperative records and surgical reports for all patients. For those undergoing coronary artery bypass grafting (CABG), details regarding the number and types of grafts (arterial and venous) and the use of specific conduits—including the left internal mammary artery (LIMA), right internal mammary artery (RIMA), saphenous vein grafts (SVG), and radial artery—were recorded. The completeness of arterial revascularization and whether the operation was urgent or a redo procedure were also noted.

For patients undergoing valve surgery, information was documented on the type and number of valves repaired or replaced, including aortic valve replacement (AVR), mitral valve replacement or repair (MVR), tricuspid valve repair or replacement (TVR), and double valve replacement (DVR). Less frequent complex operations, such as the Bentall procedure and pulmonary valve replacement (PVR), were also included.

Pre-existing hallucinations were ascertained before surgery from two sources: (1) electronic medical records (problem lists, prior inpatient/outpatient notes including psychiatry/neurology, discharge summaries, and long-term medications) and (2) family/caregiver history when available. Any positive or uncertain information was referred for psychiatric review. Patients with a confirmed history of recurrent or non-acute hallucinations were excluded. No validated screening questionnaire was used for this ascertainment.

Eligibility for interview

QPE assessments were performed only when patients were fit for interview, defined a priori as: extubated, off procedural sedation, awake with spontaneous eye opening, oriented to person, place, and time, and able to follow a three-step command. Interview readiness was verified by the ICU team before each assessment. If the criteria were not met, the interview was deferred and re-attempted later within the 7-day window.

Primary and secondary outcomes

The primary outcomes were the incidence of postoperative visual and auditory hallucinations within the first 7 days after surgery, defined as new perceptual experiences (seeing or hearing things not present) during full wakefulness. Hallucinations were assessed daily from postoperative day 1 through 4 using the **validated Arabic** Questionnaire for Psychotic Experiences (QPE) **without content modification**, and by clinical or telephone follow-up until day 7. **To ensure valid self-report in the ICU, QPE interviews were conducted only when patients were post-extubation, awake, oriented to person and place, and able to follow a three-step command; assessors used standardized prompts after centralized training with periodic calibration across centers. The QPE is a symptom-level measure (phenomenology of hallucinations) and is not a diagnostic tool for delirium; it has been applied in perioperative cardiac surgery cohorts to characterize postoperative hallucinations.** The day of onset was recorded for each patient. Severity of hallucinations, a secondary outcome, was measured using the QPE hallucination rating subscale (intensity, duration, emotional distress, and insight; each 0–5, total 0–20; higher scores indicate greater severity) (26). **Internal consistency within our cohort was acceptable (Cronbach's α: visual = 0.86; auditory = 0.71). For clarity, QPE functional-interference items were summarized descriptively and were not entered into regression models.** For Detailed Description of Outcomes and Assessments, See eAppendix 2 in Supplementary(21)**.**

To reduce misclassification attributable to postoperative debility or sedation, QPE interviews were performed only when patients could communicate reliably, that is, after extubation, awake, oriented to person and place, and able to follow a three-step command. If these conditions were not satisfied, the assessment was deferred until they were. Functional-interference items were recorded for descriptive context and were not used as predictors or outcomes in regression models.

Statistical analysis

In our study, we aimed to compare predictors between cohorts of patients who experienced visual hallucinations and those who did not experience hallucinations following cardiac surgery. To determine the necessary sample size, we utilized a two-sample independent means t-test, setting a two-sided significance level (α) at 0.05 and targeting a statistical power of 0.80 to detect a meaningful difference in LVEF between the groups. Based on previous studies

(22), we estimated the mean LVEF to be approximately 56.0% for patients without hallucinations and 51.9% for those with visual hallucinations, with standard deviations of 3.61% and 4.61%, respectively. Our calculations indicated that a total sample size of 32 participants, with 16 in each group, would be sufficient to achieve our study objectives.

Because ICU debility, sedation exposure, and fluctuating consciousness may influence patient-reported functioning, multivariable Cox models prespecified covariates that proxy these states. Adjusted models included age, sex, BMI, diabetes, EuroSCORE II, left-ventricular ejection fraction (LVEF), procedural duration, cardiopulmonary bypass time, aortic cross-clamp time, postoperative ventilation duration, postoperative blood transfusion, vasoactive exposures (norepinephrine/noradrenaline, epinephrine/adrenaline, dobutamine), immunosuppressant use, and redo surgery. Functional-interference items from the QPE were summarized descriptively and excluded from inferential models.

All statistical analyses were conducted using STATA version 17. A two-sided p-value < 0.05 was considered indicative of statistical significance. Continuous variables were presented as means ± standard deviations or medians with interquartile ranges (Q1–Q3), while categorical variables were expressed as frequencies and percentages. Baseline comparisons between groups were performed using independent samples t-tests or Mann–Whitney U tests for continuous variables, and chi-square or Fisher's exact tests for categorical variables, as appropriate.

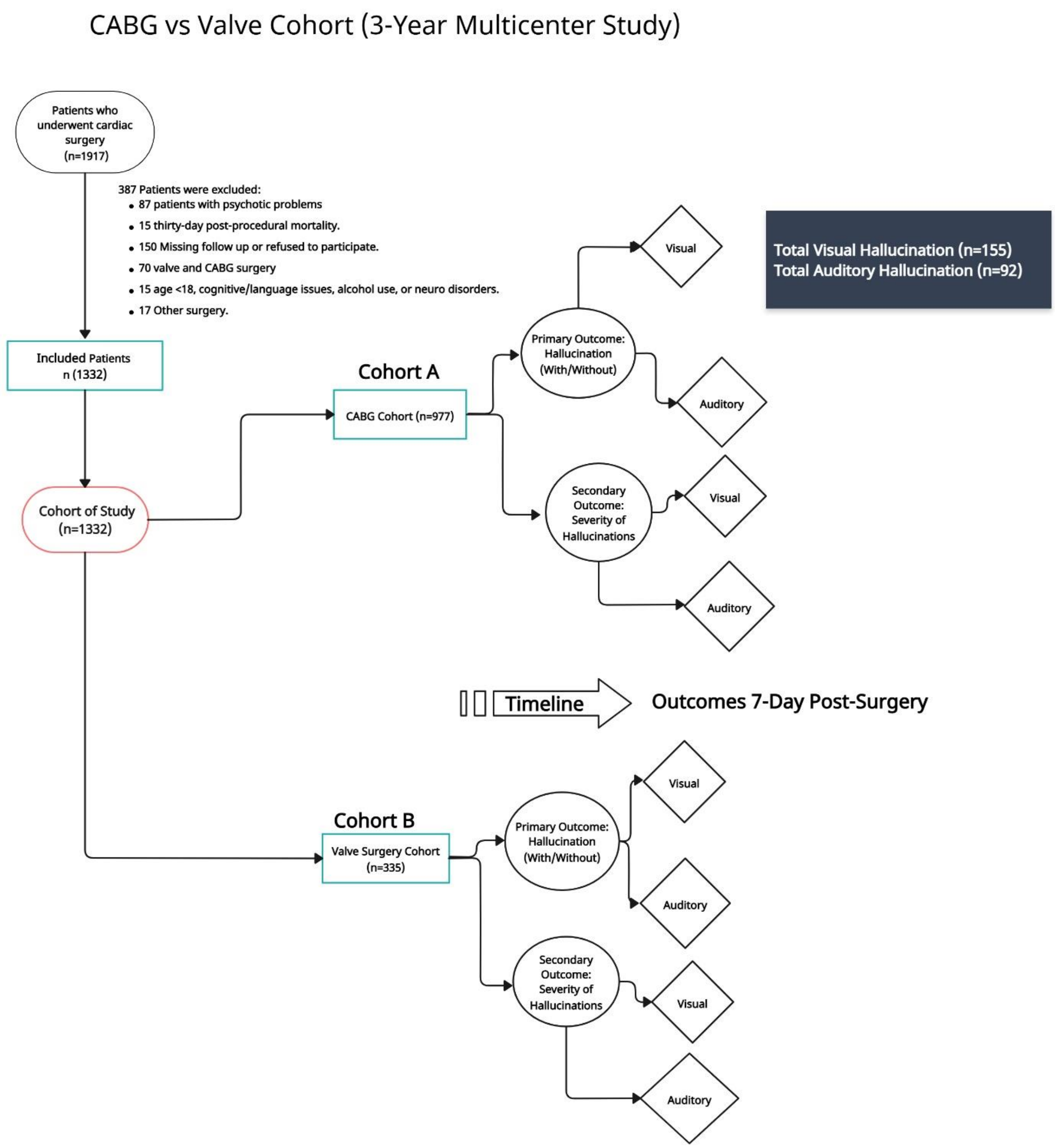
We used time-to-event analysis to evaluate the occurrence of postoperative hallucinations, treating the time to first hallucination (of each type) as the outcome. Patients who did not experience a given type of hallucination within 7 days were right-censored at the time of hospital discharge or on postoperative day 7, whichever came first. Separate Kaplan-Meier curves were generated for visual and auditory hallucinations, stratified by surgical group (CABG vs valve). For risk factor analysis, we fitted Cox proportional hazards regression models for the hazard of experiencing a hallucination. Given the substantial clinical differences between CABG and valve patients, we performed analyses within each surgical cohort rather than pooling them to allow identification of group-specific predictors (this approach corresponds to Tables 2 and 3 for CABG and valve groups, respectively). Candidate covariates for the multivariable models were chosen based on clinical relevance and prior evidence in the literature regarding delirium or neurocognitive complications after cardiac surgery (17,23–25). In particular, we considered variables such as age, sex, baseline comorbidities (e.g. diabetes, hypertension), LVEF, CPB duration, aortic cross-clamp time, intraoperative transfusions, and use of vasoactive drugs. We also included the use of immunosuppressive or corticosteroid medications. To account for potential variability in perioperative practices and monitoring protocols across the ten participating centers, all multivariable Cox regression models were stratified by hospital. This stratification allowed the baseline hazard to vary across institutions while maintaining common covariate effects, thereby controlling for unmeasured center-level heterogeneity without inflating the number of covariates. Hospital codes and patient distributions are detailed in Supplementary File 2, eTable 2.

Initially, univariable Cox analyses were run for each predictor to screen for associations. Variables with $p<0.10$ in univariable analysis, as well as those considered a priori important (age, sex, CPB use, etc.), were entered into the multivariable Cox model for each cohort. The final adjusted Cox models (one for CABG patients and one for valve patients) thus included the following covariates: age, sex, body mass index, diabetes status, LVEF, aortic cross-clamp time, CPB duration, Hemostasis at closure, need for any transfusion (yes/no), use of vasopressors/inotropes (norepinephrine, epinephrine, etc.), and use of immunosuppressive therapy. This allowed us to estimate the independent effect of each factor on hallucination risk while controlling for potential confounders. We checked proportional hazards assumptions using Schoenfeld residuals; no major violations were detected. Hazard ratios (HRs) with 95% confidence intervals were reported. Model construction followed the Transparent Reporting of a Multivariable Prediction Model for Individual Prognosis or Diagnosis (TRIPOD) criteria (26).

Ethical considerations

The study was approved by the IRB of An-Najah National University and participating hospitals. Written informed consent was obtained, and data were anonymized and securely stored.

Figure 1: Flow Chart. CABG vs. Valve Groups (CABG: Coronary Artery Bypass Grafting


CABG vs Valve Cohort (3-Year Multicenter Study)
Patients who underwent cardiac surgery (n=1917)
387 Patients were excluded:
87 patients with psychotic problems
15 thirty-day post-procedural mortality.
150 Missing follow up or refused to participate.
70 valve and CABG surgery
15 age <18, cognitive/language issues, alcohol use, or neuro disorders.
17 Other surgery.
Included Patients n (1332)
Cohort of Study (n=1332)
Cohort A
CABG Cohort (n=977)
Primary Outcome: Hallucination (With/Without)
Visual
Auditory
Secondary Outcome: Severity of Hallucinations
Visual
Auditory
Total Visual Hallucination (n=155)
Total Auditory Hallucination (n=92)
Timeline
Outcomes 7-Day Post-Surgery
Cohort B
Valve Surgery Cohort (n=335)
Primary Outcome: Hallucination (With/Without)
Visual
Auditory
Secondary Outcome: Severity of Hallucinations
Visual
Auditory

Results

A total of 1,332 patients were included in the final analysis, comprising 997 who underwent isolated coronary artery bypass grafting (CABG) and 335 who underwent valve surgery. Table 1 summarizes the surgical characteristics of the cohort. Among CABG patients, the mean number of grafts was 3.2 ± 0.9, and the left internal mammary artery (LIMA) and saphenous vein graft (SVG) were the most frequently used conduits. In contrast, among valve surgery cases, the most common procedure was aortic valve replacement (AVR), followed by mitral valve replacement or repair (MVR). Combined procedures, such as double valve replacement, were less frequent.

Table 1. Surgical Descriptive Characteristics (N = 1332)

Variable	**n (%) or Mean ± SD**
Coronary artery bypass grafting (CABG) procedures (N = 997)	
Number of grafts	**3.21 ± 0.93**
1 graft	**48 (4.8 %)**
2 grafts	**143 (14.3 %)**
3 grafts	**454 (45.5 %)**
4 grafts	**265 (26.6 %)**
5 grafts	**87 (8.7 %)**
Total	**997 (100 %)**
LIMA used	**869 (87.2 %)**
RIMA used	**196 (19.7 %)**
SVG used	**747 (74.9 %)**
Radial artery used	**146 (14.6 %)**
Valve surgery procedures (N = 335)	
Aortic valve replacement (AVR)	**277 (82.7 %)**
Mitral valve replacement/repair (MVR)	**168 (50.1 %)**
Tricuspid valve repair/replacement (TVR)	**58 (17.3 %)**
Double valve replacement (DVR)	**96 (28.7 %)**
(note: totals > 100 % because some patients had combined valve procedures)	

Definitions and Notes:LIMA = Left internal mammary artery graft; RIMA = Right internal mammary artery graft; SVG = Saphenous vein graft; Radial artery used = use of radial artery as conduit; Total arterial graft = complete arterial revascularization (LIMA ± RIMA without SVG);

AVR = Aortic valve replacement; MVR = Mitral valve replacement or repair; TVR = Tricuspid valve repair/replacement; DVR = Double (aortic + mitral) valve replacement.

Regarding clarity and conciseness, eTable 1 (titled 'Clinical Characteristics of Visual and Auditory Hallucinations After Cardiac Surgery') has been moved to Supplementary File 1.

eTable 1 shows the frequency, duration, content, and impact of hallucinations in CABG (n=997) and valve replacement (n=335). In CABG, visual hallucinations were rare (1.7%), brief (88.6%), non-distressing (93.0%), and with preserved insight (97.3%). By contrast, auditory hallucinations were more frequent (54.0% daily; 35.1% hourly), longer (32.4% minutes; 4.0% continuous), distressing (8.1% severe anxiety; 17.5% convinced real), with functional impact in 31.1% and crisis support in 2.7%.

In valve patients, visual hallucinations (11.6%) were more complex (51.2% persons/animals; 25.6% objects) and sometimes continuous (10.2%). Auditory hallucinations (2.7%) were structured (27.7% short phrases; 27.7% several sentences), often negative (22.2%), with impaired insight in 41.1% and severe distress in 11.1%.

Regarding clarity and conciseness, eTable 2 (titled 'Visual Hallucinations and Their Association with Demographic, Clinical, Laboratory, and Procedural Variables in Patients Undergoing Coronary Artery Bypass Grafting and Valve Surgery') has been moved to Supplementary File 1.

eTable 2 shows perioperative variables associated with visual hallucinations in CABG (n=997) and valve surgery (n=335). In CABG, 116 patients (11.6%) reported hallucinations, linked to immunosuppressive drug use (36.4% vs. 7.4%, p=0.02) and dobutamine (6.0% vs. 1.9%, p=0.015), with trends for recent MI (29.5% vs. 22.7%, p=0.09) and hyperlipidemia (44.3% vs. 36.1%, p=0.07).

In the valve cohort, 39 patients (11.6%) had hallucinations, associated with hemodialysis (10.3% vs. 1.4%, p=0.008), immunosuppressive therapy (7.7% vs. 1.4%, p=0.037), and longer ventilation (6.26 h, IQR 1.47–11.05 vs. 4.18 h, IQR 2.30–6.06; p=0.034).

Figure 2. Cumulative Incidence of Visual and Auditory Hallucinations Following Cardiac Surgery

A) Visual hallucinations

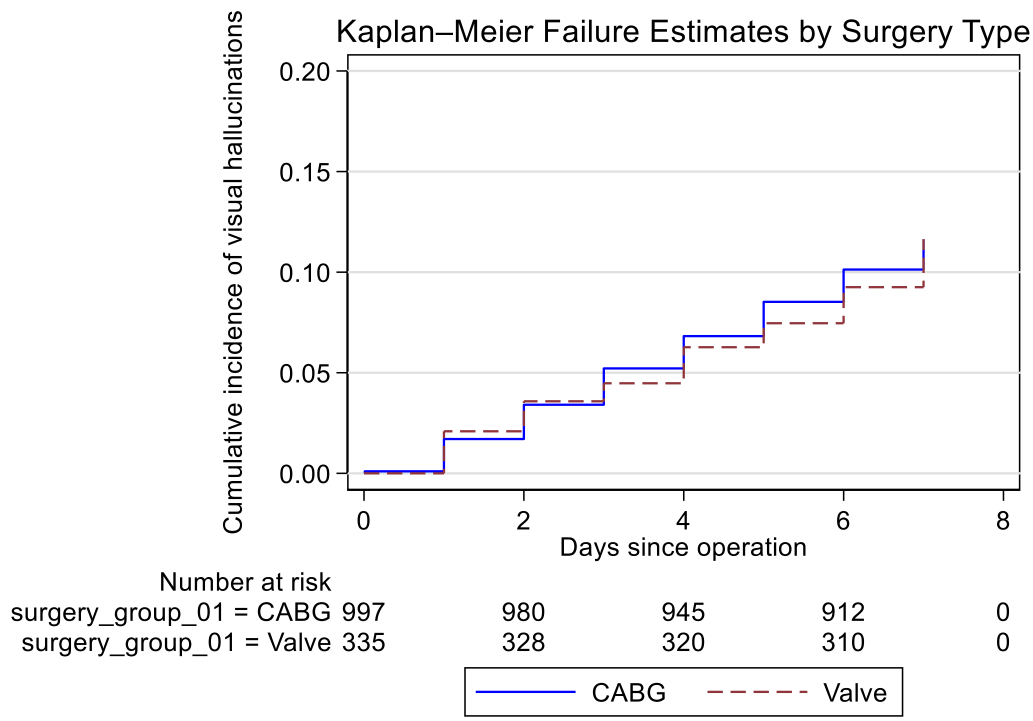


Figure 2A. Cumulative incidence of visual hallucinations during the first seven postoperative days in patients undergoing CABG (solid blue line) and valve surgery (dashed red line). Incidence increased over time, reaching ~11% in CABG and ~10% in valve patients by day seven. The CABG group consistently showed a slightly higher incidence, suggesting visual hallucinations are common post-cardiac surgery and may be marginally more frequent after CABG, possibly due to perioperative factors, sedation practices, or intraoperative stress.

B) Auditory hallucinations

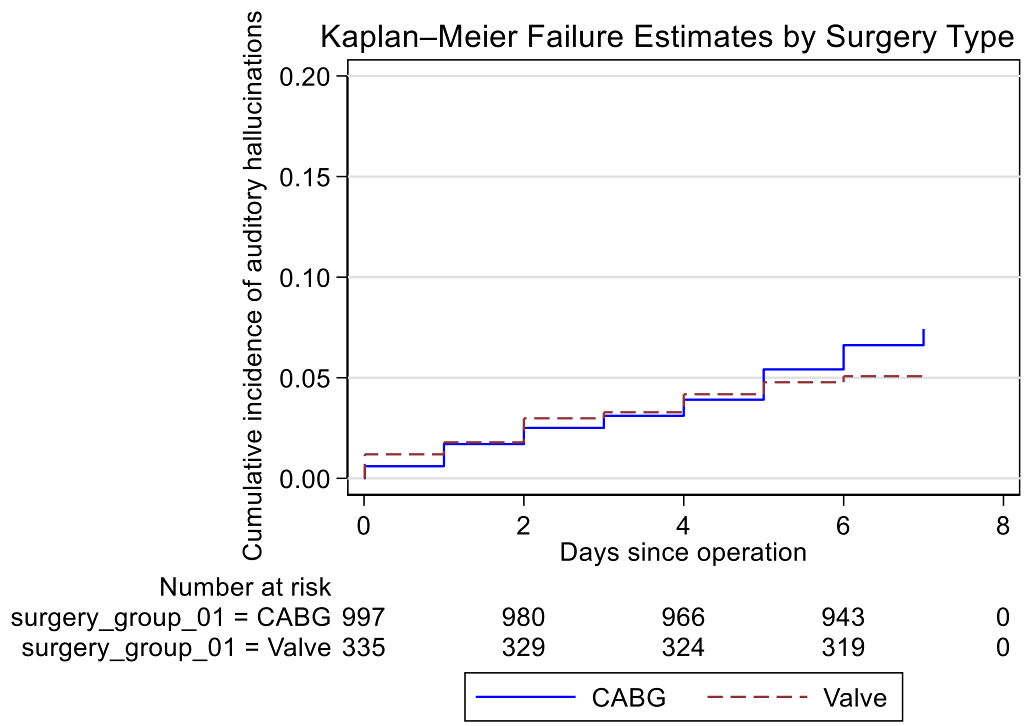


Figure 2B. Cumulative incidence of auditory hallucinations during the first seven postoperative days in CABG (solid blue line) and valve surgery (dashed red line). Incidence rose gradually, with CABG patients consistently higher, reaching ~7% versus 5% in valve patients by day seven. Auditory hallucinations are less frequent than visual but not uncommon, and the higher CABG incidence may reflect intraoperative management, sedation, or patient risk profiles, highlighting targets for perioperative neuropsychiatric risk assessment.

Regarding clarity and conciseness, eFigure1 (titled 'Distribution and Severity of Postoperative Visual and Auditory Hallucinations Stratified by Surgery Type') has been moved to Supplementary File 1.

The severity of postoperative hallucinations varied by type and surgical group. As shown in eFigure 1, auditory hallucinations were more severe, with median scores of 6 (IQR: 4–10) for CABG and 6.5 (IQR: 5–12) for valve surgeries. Visual hallucinations were generally milder, with medians of 3 (IQR: 1–6.5) in CABG and 3 (IQR: 1–6) in valve patients. Auditory scores had moderate positive skewness (CABG: 0.89, Valve: 0.99), while visual scores were more skewed (CABG: 1.19, Valve: 1.04), showing a non-normal distribution with clustering at lower severity and a long tail toward higher scores. These findings indicate auditory hallucinations are typically more severe and support non-parametric visualization in eFigure 1. **For detailed**

descriptive statistics, including percentiles and distribution characteristics, please refer to Supplementary 1 eTables 4–7.

Regarding clarity and conciseness, eTable 3 (titled 'Associations Between Auditory Hallucinations and Perioperative Variables Following CABG and Valve Surgery') has been moved to Supplementary File 1.

eTable 3 shows associations between auditory hallucinations and perioperative factors. In the CABG cohort (n=997), hallucinations were linked to lower LVEF (52.0% vs. 53.9%, p=0.021), longer cross-clamp times (82.3 vs. 73.0 min, p=0.034), and longer ventilation (median 5.32 h, IQR 2.58–8.06 vs. 4.14 h, IQR 2.46–5.83, p=0.014), suggesting impaired cardiac function and prolonged support increase risk.

In the valve cohort (n=335), patients with hallucinations had higher EuroSCORE II (median 9.57, IQR 1.15–20.29 vs. 3.31, IQR 1.90–4.72, p<0.001) and were more likely to receive adrenalin (72.2% vs. 42.6%, p=0.025) and noradrenalin (83.3% vs. 55.5%, p=0.026). Other demographics and comorbidities showed no significant differences.

Details of immunosuppressive therapy and hospital distribution are provided in Supplementary File 2. Specifically, eTable 1 summarizes the types and pharmacologic classes of immunosuppressive drugs recorded in the cohort, while eTable 2 lists anonymized hospital codes and their respective patient distributions across the ten participating centers.

Table 2. Predictors of Visual and Auditory Hallucinations Following Coronary Artery Bypass Grafting: Univariate and Multivariate Cox Regression Analysis

	Cohort A: CABG(n=997)							
	Visual				**Auditory**			
Predictors	**Crude HR(%95 CI)**	**Crude P Value**	**adjusted HR (%95 CI)***	**adjusted P Value***	**Crude HR(%95 CI)**	**Crude P Value**	**adjusted HR(%95 CI)***	**adjusted P Value***
Age	1.01 (0.99–1.03)	0.348	1.01 (0.99–1.04)	0.250	0.98 (0.95–1.01)	0.100	0.98 (0.95–1.00)	0.062
Male	1.13 (0.71–1.80)	0.603	1.09 (0.67–1.76)	0.731	1.11 (0.62–1.99)	0.722	1.00 (0.55–1.82)	0.989
BMI, kg/m2	0.98 (0.93–1.03)	0.439	0.98 (0.93–1.03)	0.408	1.01 (0.95–1.06)	0.808	1.02 (0.96–1.07)	0.570
Diabetes	1.06 (0.73–1.52)	0.765	1.04 (0.71–1.52)	0.831	1.32 (0.83–2.10)	0.242	**1.66 (1.01–2.73)**	**0.044**
Left ventricle ejection fraction, %	1.01 (0.98–1.03)	0.671	1.01 (0.98–1.04)	0.731	1.05 (1.01–1.09)	0.019	**1.05 (1.01–1.09)**	**0.012**
Cardiopulmonary bypass time, min	1.00 (1.00–1.01)	0.521	1.00 (0.99–1.01)	0.294	0.99 (0.99–1.00)	0.495	0.99 (0.99–1.00)	0.067
Aortic cross clamp time, min	1.00 (0.99–1.01)	0.791	1.00 (0.99–1.01)	0.469	1.00 (1.00–1.01)	0.451	**1.01 (1. CI1.0004–1.02)**	**0.022**
Hemostasis at closure, Adequate vs Poor	0.71(0.48–1.03)	0.07	0.81 (0.45–1.43)	0.462	0.78(0.48–1.26)	0.321	1.04 (0.54–2.01)	0.915
Post operative ventilation	0.99 (0.95–1.04)	0.694	0.99 (0.95–1.04)	0.654	1.01 (0.98–1.04)	0.498	1.01 (0.98–1.04)	0.676

Post-operative Receiving blood transfusion	1.87 (1.05–3.33)	0.034	**1.97 (0.95–4.09)**	**0.068**	0.81 (0.30–2.22)	0.683	0.74 (0.23–2.34)	0.602
Euroscore II	0.97 (0.85–1.10)	0.616	0.97 (0.85–1.10)	0.626	0.97 (0.85–1.10)	0.865	1.01 (0.92–1.11)	0.760
Adrenalin	0.84 (0.58–1.21)	0.348	0.75 (0.48–1.16)	0.194	0.84 (0.58–1.21)	0.111	0.76 (0.44–1.32)	0.326
Dobutamin	0.34 (0.05–2.47)	0.289	0.30 (0.04–2.24)	0.241	0.56 (0.08–4.00)	0.559	0.40 (0.05–3.02)	0.378
Immunosuppressive drugs	0.76 (0.11–5.43)	0.783	0.49 (0.06–3.67)	0.485	2.72 (0.67–11.10)	0.162	4.05 (0.88–18.76)	0.073
Redo Surgery	1.32 (0.58–3.00)	0.509	1.39 (0.58–3.30)	0.459	0.31 (0.04–2.23)	0.244	0.31 (0.04–2.27)	0.247

CABG, coronary artery bypass grafting; BMI, body mass index; LVEF, left ventricular ejection fraction; HR, hazard ratio; CI, confidence interval;* , stratified by Hospital.

Table 2 summarizes predictors of postoperative hallucinations among CABG patients (n = 997). In multivariable analyses stratified by hospital, no demographic or operative variables significantly predicted visual hallucinations. The previously observed univariate effect of blood transfusion (HR 1.87, p = 0.034) was attenuated after adjustment (HR 1.97, p = 0.068).

For auditory hallucinations, higher left ventricular ejection fraction (HR 1.05, 95% CI 1.01–1.09, p = 0.012), longer aortic cross-clamp time (HR 1.01, 95% CI 1.0004–1.02, p = 0.022), and diabetes (HR 1.66, 95% CI 1.01–2.73, p = 0.044) were significant predictors. Immunosuppressive therapy showed a borderline association (HR 4.05, 95% CI 0.88–18.76, p = 0.073). Other factors, including age, BMI, and vasoactive medications, were not significantly associated.

Table 3. Predictors of Visual and Auditory Hallucinations Following Valve Surgery: Univariate and Multivariate Cox Regression Analysis

	Cohort B: Valve Surgery(n=335)							
	Visual				Auditory			
Predictors	**Crude HR(%95 CI)**	**Crude P Value**	**adjusted HR(%95 CI) ***	**adjusted P Value ***	**Crude HR(%95 CI)**	**Crude P Value**	**adjusted HR(%95 CI) ***	**adjusted P Value ***
Age	0.998 (0.976–1.020)	0.848	1.00 (0.98–1.03)	0.738	0.99 (0.96–1.02)	0.392	0.98 (0.94–1.02)	0.369
Male	1.28 (0.68–2.41)	0.435	1.76 (0.88–3.50)	0.110	0.88 (0.35–2.23)	0.791	0.98 (0.37–2.65)	0.974
BMI, kg/m2	0.98 (0.90–1.06)	0.532	**0.90 (0.81–1.00)**	**0.061**	1.03 (0.94–1.13)	0.564	1.02 (0.90–1.16)	0.739
Diabetes	0.94 (0.46–1.94)	0.875	0.96 (0.43–2.14)	0.919	1.05 (0.37–2.94)	0.927	1.06 (0.35–3.21)	0.925
Left ventricle ejection fraction, %	1.02 (0.97–1.08)	0.369	1.01 (0.97–1.06)	0.583	0.99 (0.93–1.06)	0.747	0.99 (0.93–1.04)	0.645
Cardiopulmonary bypass time, min	1.01 (1.00–1.01)	0.114	**1.01 (1.00–1.02)**	**0.097**	1.01 (1.00–1.02)	0.177	1.00 (0.98–1.02)	0.915
Aortic cross clamp time, min	1.01 (1.00–1.01)	0.202	1.70 (0.68–4.26)	0.259	1.01 (1.00–1.02)	0.080	0.94 (0.20–4.45)	0.940
Hemostasis at closure, Adequate vs Poor	0.94(0.49–1.97)	0.86	0.99 (0.98–1.01)	0.406	1.18(0.44–3.14)	0.739	1.01 (0.99–1.03)	0.356
Post operative ventilation	0.82 (0.73–0.93)	0.002	**0.78 (0.68–0.90)**	**0.001**	0.97 (0.86–1.09)	0.599	0.97 (0.87–1.08)	0.552

Post-operative Receiving blood transfusion	1.76 (0.69–4.49)	0.240	1.21 (0.40–3.66)	0.731	1.44 (0.33–6.28)	0.625	1.83 (0.33–10.26)	0.494
Euroscore II	0.93 (0.71–1.21)	0.597	0.91 (0.70–1.17)	0.457	0.94 (0.66–1.35)	0.749	0.92 (0.59–1.43)	0.697
Noradrenalin	2.27 (1.10–4.65)	0.026	**6.07 (2.18–16.93)**	**0.001**	3.86 (1.12–13.32)	0.033	3.48 (0.68–17.88)	0.136
Adrenalin	1.36 (0.72–2.54)	0.340	0.60 (0.23–1.55)	0.292	3.40 (1.21–9.54)	0.020	2.50 (0.61–10.20)	0.201
Dobutamin	0.47 (0.06–3.44)	0.459	0.38 (0.04–3.19)	0.371	1.12 (0.15–8.42)	0.912	0.91 (0.10–8.55)	0.937
Immunosuppressive drugs	5.01 (1.54–16.30)	0.007	**5.13 (1.14–23.09)**	**0.033**	2.88 (0.38–21.66)	0.304	2.62 (0.20–35.02)	0.466
Redo Surgery	1.86 (0.82–4.21)	0.137	1.58 (0.64–3.90)	0.322	1.59 (0.46–5.50)	0.462	0.93 (0.25–3.52)	0.917

HR, hazard ratio; CI, confidence interval; BMI, body mass index; LVEF, left ventricular ejection fraction; *, stratified by Hospital.

Table 3 summarizes the Cox regression analyses for predictors of postoperative hallucinations in valve surgery patients (n = 335). Prolonged postoperative ventilation was independently associated with a lower risk of visual hallucinations (adjusted HR 0.78, 95% CI 0.68–0.90, p = 0.001), while noradrenaline administration markedly increased the risk (adjusted HR 6.07, 95% CI 2.18–16.93, p = 0.001). Immunosuppressive therapy was also a significant predictor (adjusted HR 5.13, 95% CI 1.14–23.09, p = 0.033).

For auditory hallucinations, none of the covariates reached statistical significance after adjustment; however, noradrenaline (HR 3.48, p = 0.136) and adrenaline (HR 2.50, p = 0.201) exposure showed upward trends, suggesting potential catecholamine-related risk mechanisms. These associations are illustrated in eFigure 2, which displays the adjusted hazard ratios for both visual and auditory outcomes.

Regarding clarity and conciseness, eFigure 2 (titled 'Adjusted Hazard Ratios for Visual and Auditory Hallucinations Following Cardiac Surgery (CABG and Valve Surgery) in 1,332 Patients') has been moved to Supplementary File 1.

This figure combines two subplots: eFigure 2A shows HRs for visual hallucinations by surgery type; eFigure 2B shows HRs for auditory hallucinations by surgery type. Confidence intervals with extreme values were truncated for clarity and comparison HRs >1 indicate a higher risk of hallucinations associated with a given variable, while HRs <1 suggest protective effects. Key predictors include postoperative transfusion and LVEF for CABG, and noradrenaline use and ventilation for valve surgery.

Discussion:

Summary of Key Findings and Incidence Patterns

In this multicenter prospective cohort of 1,332 patients undergoing CABG or valve surgery across West Bank centers, we assessed incidence, timing, and perioperative predictors of postoperative visual and auditory hallucinations. Using the validated Questionnaire for Psychotic Experiences (QPE) and robust follow-up over the first seven postoperative days, visual hallucinations occurred in 11.5% of CABG and 10.0% of valve patients, while auditory hallucinations were observed in 7.0% and 5.0%, respectively. Kaplan-Meier analysis showed hallucinations typically appeared within the first few postoperative days, with visual hallucinations more frequent but transient, and auditory hallucinations less common yet more distressing. Multivariable Cox regression identified key predictors, including postoperative transfusions (CABG), reduced left ventricular ejection fraction LVEF, aortic cross-clamp time, and use of immunosuppressants and catecholamines (notably noradrenaline) in valve patients. These results indicate hallucinations are influenced by identifiable, often modifiable clinical factors.

Clinical Burden and Implications of Postoperative Hallucinations

Postoperative hallucinations, though often under-recognized, impose a significant neuropsychiatric burden on cardiac surgery patients (27). Visual and auditory hallucinations may be misinterpreted as psychosis or delirium, prompting unnecessary medications, increased monitoring, or prolonged ICU stays. Such neuropsychiatric events are linked to lower patient satisfaction, delayed recovery, and higher rates of anxiety, post-traumatic stress, and long-term cognitive decline (28,29). Our findings support that hallucinations are not benign, particularly in high-risk CABG or valve surgery patients. Early identification of patients requiring inotropes or post-operative transfusions enables proactive intervention. Non-pharmacological strategies, careful sedative titration, early mobilization, and reorientation should be prioritized. Recognizing hallucinations as distinct from delirium is crucial: evidence shows 77% of post-cardiac surgery patients with hallucinations do not develop delirium (30), highlighting the need for tailored evaluation rather than default delirium management.

CABG cohort

Visual hallucinations were strongly associated with post-operative blood transfusions. Consistent with Ottens et al., transfused patients had a higher risk of postoperative hallucinations (crude OR 2.08, 95% CI 1.04–4.16) (31). This may reflect transfusion-induced inflammation, as studies show increased interleukin 6 (IL-6) levels post-transfusion (24), likely due to cell-free hemoglobin accumulation in stored blood. Cell-free hemoglobin binds nitric oxide, reducing vascular protection, increasing permeability, and allowing inflammatory mediators to cross the blood-brain barrier, particularly affecting the hippocampus, which contributes to visual hallucinations (32). These findings support a role for transfusion-related neuroinflammation in postoperative visual hallucinations.

On the other hand, we observe that auditory hallucinations were associated with a distinct set of predictor factors, most notably reduced left ventricular ejection fraction. This finding differed from Ottens et al. and Tschernatsch et al., who demonstrated no statistical significance between hallucinations and reduced LVEF (31)(33). These discrepancies may be attributed to differences in population characteristics and the degree of LVEF reduction. Nonetheless, Parente et al. identified heart failure as an independent risk factor of post-operative delirium, supporting our findings. This relationship could be attributed to the neurohormonal activation in heart failure and reduced LVEF. As a compensatory mechanism of decreased cardiac output, the renin-angiotensin-aldosterone system (RAAS) is activated, elevating angiotensin II and aldosterone levels, which lead to vasoconstriction that reduces perfusion to various organs, including the brain. Specifically, this mechanism diminishes cerebral metabolism and perfusion, which has been shown to contribute to the development of cognitive impairment and, therefore, hallucinations (34)(35). Moreover, Auditory hallucinations also showed a significant association with longer aortic clamp time. This supports the idea that cerebral hypoperfusion contributes to the development of neurocognitive disturbances. Similarly, Tschernatsch et al. reported a positive correlation between this variable and pseudohallucinations (33). Additionally, they portrayed a significant bivariate correlation with extracorporeal circulation (ECC) ($p = 0.048$), similar to Ottens et al., who showed a substantial association between post-operative hallucinations and cardiopulmonary bypass duration (crude OR 1.005 per minute, 95% CI 1.00

to 1.01, p = 0.075) (31). Although this variable was not found to be significant in our study, these findings could suggest that mechanisms specific to on-pump surgery may contribute to the development of cognitive dysfunction. Upon the initiation of cardiopulmonary bypass, the brain is exposed to a period of hypoperfusion due to a low mean arterial pressure. Although cardiac output is maintained with the CPB, low mean arterial pressure may be caused by the manipulation of the great vessels, heart, or lungs. This specifically reduces blood flow to watershed areas such as the hippocampus, contributing to cognitive dysfunction (36).

Interestingly, a significant association was identified between auditory hallucinations and the use of immunosuppressive drugs. Generally, cognitive impairment has been reported in studies after the administration of immunosuppressive medications. More specifically, calcineurin inhibitors (CNI) were found to cause avid neurotoxicity by binding to low-density lipoproteins and increasing their permeability through the blood-brain barrier. Additionally, these drugs caused elevated endothelin levels, playing a role in the development of endothelial dysfunction, vasoconstriction, and cerebral vasospasm. The mitochondrial dysfunction caused by CNIs leads to the formation of free radicals, which can lead to apoptotic or necrotic cell death (37). While these mechanisms have explained the development of neuropsychiatric side effects, there is no reported literature on the association with post-cardiac surgery hallucinations. Case reports have described hallucinations in patients who were administered immunosuppressive therapy, yet this relationship has not been explained in the context of cardiac surgeries. This suggests the need for further studies on the underlying mechanism of this association (38).

Other variables, such as age, diabetes, post-operative ventilation, and adrenaline, were not found to be significant in our study. These findings are consistent with Ottens et al., who showed no significant association between post-operative hallucinations and either age or diabetes, suggesting that post-operative hallucinations may be more closely linked with intraoperative events rather than pre-existing comorbidities (31). However, our findings regarding CABG surgery suggest that types of post-CABG hallucinations are associated with different underlying factors. While visual hallucinations appeared to be associated with inflammatory triggers, auditory hallucinations were more closely related to factors affecting cerebral hypoperfusion. This novel notion could contribute to shaping preventive strategies in patients undergoing cardiac surgery.

Valve cohort

Regarding patients who underwent valve surgery, the predictor factors of postoperative hallucination were divided into patient-specific, surgical, and medication-related. One significant factor found to increase the likelihood of developing hallucinations is noradrenaline use, which has been associated with an increased occurrence of both visual and auditory hallucinations. To the best of our knowledge, no study has specifically investigated the effect of noradrenaline on the risk of developing hallucinations following cardiac surgery. Increased noradrenaline activity has been implicated in the development of hallucinations, particularly under stress (39). The locus coeruleus-noradrenaline system plays a key role in arousal and attention, and stress-induced stimulation of low-affinity alpha-1 noradrenaline receptors impairs prefrontal cortex function, reducing the brain's ability to filter irrelevant stimuli and increasing vulnerability to hallucinations (39)(40). In addition, high levels of arousal impair attentional selectivity, reducing the ability to distinguish relevant information from distracting noise (39). Therefore, the pharmacologic administration of noradrenaline, which further stimulates the adrenergic system, may exacerbate this dysfunction, intensifying hyperarousal, impairing attentional selectivity, and increasing the likelihood of hallucinations in predisposed individuals. On the other hand, adrenaline administration, which was significantly associated with auditory hallucinations in univariate analysis, may act through a similar stress-related mechanism as noradrenaline. However, the lack of statistical significance in the adjusted model suggests that this association may be confounded by other clinical variables. Niccol et al. found that a significant portion of patients who developed hallucinations in the ICU were critically ill individuals who had received vasopressors such as adrenaline and noradrenaline (41). This suggests that the hallucinations may be better explained by the neurocognitive dysfunction associated with critical illness or the effects of polypharmacy in these patients, rather than a direct pharmacologic effect of adrenaline itself.

Another pharmacologic association was observed with immunosuppressive drugs, which appeared to increase the risk of visual hallucinations in patients following valvular surgeries, showing statistical significance in the univariate analysis and a near-significant trend in the multivariate model. Despite the absence of research specifically addressing the risk of immunosuppressive medications in the development of hallucinations after valvular surgeries, some reports have indicated an association between these drugs and psychotic symptoms, including hallucinations, in the context of non-cardiac surgeries (42)(43), One possible explanation for this association is that Calcineurin inhibitors such as tacrolimus and cyclosporine are lipophilic drugs that can cross the blood brain barrier and disrupt central nervous system integrity. Their neurotoxic effects may lead to vasogenic edema, altered neurotransmitter signaling, and in some cases, posterior reversible encephalopathy syndrome. Hallucinations are one of the recognized neuropsychiatric manifestations of this drug-induced toxicity, occurring in approximately 5% of patients who receive these drugs (44)(45). Corticosteroids, on the other hand, have been implicated in disrupting the hypothalamic–pituitary–adrenal axis, leading to dysregulation of stress responses and alterations in neurotransmitter levels, particularly dopamine, serotonin, and glutamate. These changes can result in a range of neuropsychiatric manifestations, one of which is hallucinations (44).

The only factor found to be significantly protective against visual hallucinations following valvular surgery in our study was **prolonged postoperative ventilation**. This finding may be explained by the fact that longer ventilation typically necessitates deeper sedation, which could mitigate the occurrence of hallucinations by reducing sensory overstimulation and promoting a smoother recovery process, and thus preventing agitation during the critical postoperative period. However, Ottens et al. demonstrated that the cumulative postoperative use of sedative medications, including benzodiazepines and opioids, was not significantly associated with the development of hallucinations after cardiac surgery (including both valvular surgeries and CABG) upon multivariate analysis. Specifically, cumulative benzodiazepine dose (IV midazolam equivalent) showed no significant association (OR 0.998, 95% CI 0.99–1.01, p=0.773), nor did cumulative opioid dose (IV morphine equivalent), with an OR of 1.007 (95% CI 0.99–1.02, p=0.371). In contrast, Teller et al. identified increased intraoperative sedative use as a significant risk factor for postoperative hallucinations in patients undergoing cardiac surgery or percutaneous valve replacement, based on univariate analysis (p=0.029)(15) . The difference between our findings and prior studies may partly stem from the deeper sedation used with prolonged ventilation. This level of sedation could impair patients' awareness or recall of hallucinations, leading to underreporting. As a result, the perceived protective effect observed in our study might be overestimated or misleading.

The other variables examined in our study were not found to be significantly associated with the development of hallucinations following valvular surgery in either the univariate or multivariate analyses. Notably, patient age and blood product transfusion did not emerge as significant factors in our cohort. However, in contrast to our findings, Ottens et al. reported both age (OR 1.048, 95% CI 1.01–1.09, p=0.009) and post-operative transfusion of blood products (OR 2.081, 95% CI 1.04–4.16, p=0.038) as independent predictors of postoperative hallucinations (31). On the other hand, variables such as male sex, diabetes, duration of cardiopulmonary bypass, and left ventricular ejection fraction were not significantly associated with hallucinations in either study, supporting the findings of our study.

The ultimate goal of identifying risk factors for the development of hallucinations in patients undergoing valvular surgery is to allow for appropriate patient education, particularly in high-risk patients, by providing them with knowledge about the potential for postoperative hallucinations and their typically benign nature. It also enables the medical team to recognize the hallucinations early, provide appropriate reassurance, and manage the condition effectively, thereby minimizing patient distress and reducing the risk of further complications.

An important observation in our study, which is evident in prespecified subgroup analyses, is that predictors of postoperative hallucinations differed between isolated CABG and isolated valve surgery despite harmonized anesthetic and cardiopulmonary bypass protocols (47). Several pathophysiologic and procedural distinctions plausibly account for these divergent patterns. CABG patients typically present with diffuse atherosclerosis and reduced left-ventricular reserve, and the operation entails substantial aortic manipulation (cannulation, cross-clamping, proximal anastomoses), which together increase the likelihood of cerebral microembolization and watershed hypoperfusion (48). These mechanisms are consistent with our CABG-specific associations linking lower LVEF and longer cross-clamp time with auditory hallucinations. By contrast, valve procedures often produce abrupt shifts in loading conditions and more labile perioperative hemodynamics, necessitating higher catecholamine support most commonly norepinephrine and epinephrine (49). The resulting adrenergic hyperarousal and stress-response activation may promote sensory misperception (45), aligning with the vasoactive signals we observed in the valve cohort. This framework also offers a parsimonious explanation for why longer postoperative ventilation appeared protective only after valve surgery: deeper sedation may blunt catecholamine-driven hyperarousal during the most hemodynamically labile phase. While hypothesis-generating, these mechanistic differences provide a coherent rationale for the distinct hallucination profiles across the two surgical groups.

Appropriateness of the QPE in Postoperative ICU Settings

Although originally validated in psychiatric populations, the QPE functions as a symptom-based instrument rather than a diagnostic tool and has been successfully applied in cardiac surgery cohorts. In our study, the Arabic QPE demonstrated good internal consistency (Cronbach's α: visual = 0.86; auditory = 0.71) and was administered only when patients were fully alert and communicative. These findings support its appropriateness for capturing postoperative hallucination phenomenology in ICU patients, while acknowledging that it does not replace delirium-specific assessments.

Level of Consciousness and Interview Eligibility

We did not record GCS scores, as all QPE assessments were conducted only after patients were fully awake, oriented, and able to communicate, which are conditions equivalent to a GCS of 15. This pragmatic approach ensured reliable self-report, though it limits direct comparison with studies using formal GCS scoring.

Strengths

This is the first Middle Eastern multicenter, prospective cohort study on postoperative hallucinations in cardiac surgery, covering 1,332 patients across all West Bank CCU centers. The validated QPE tool ensured accurate symptom capture. The large, diverse cohort and 3-year follow-up provide strong external validity. Robust Cox regression with adjustment clarified independent predictors, while forest plots made risks clinically interpretable. Collectively, these strengths elevate the study's relevance to both science and practice.

Limitations

Observational design limits causal inference. Hallucinations relied on patient report, risking under-detection in sedated patients. Follow-up was confined to the first postoperative week, missing late or long-term effects. Long-term neuropsychiatric outcomes were not assessed. Because ascertainment relied on EMR and informant history rather than a structured tool, some misclassification of pre-existing hallucinations is possible.

Patients who experienced perioperative or postoperative shock were excluded because they were sedated or clinically unstable, ensuring that all analyzed patients were hemodynamically stable at the time of psychiatric evaluation. To account for intraoperative stability, we used hemostasis at closure as a practical indicator of operative bleeding control and perfusion adequacy. This approach allowed for a consistent adjustment of intraoperative conditions across all models. Nevertheless, we acknowledge as a limitation the absence of detailed intraoperative mean arterial pressure (MAP) recordings, which could have provided a more direct quantification of hemodynamic fluctuations.

Although the models were stratified by hospital to adjust for institutional differences in surgical and perioperative management, this approach accounts primarily for baseline hazard variation rather than specific inter-center practices. Therefore, subtle variations in anesthetic techniques, ICU protocols, or postoperative monitoring that were not captured in the dataset may still have contributed to residual confounding. Future multicenter analyses with standardized perioperative data collection are warranted to further minimize center-level variability.

QPE functional-interference ratings in ICU patients may be inflated by postoperative debility, sedation, or fluctuating arousal rather than hallucinations per se. We mitigated this by restricting interviews to communicative, oriented patients, analyzing interference items descriptively only, and adjusting for proxies of debility/sedation (e.g., ventilation duration, procedural duration, vasoactive exposure, transfusion, operative complexity, EuroSCORE II, and LVEF). Nonetheless, residual confounding cannot be excluded, and interpretations of functional impact should remain cautious.

Conclusion

In this 1,332-patient cohort, postoperative hallucinations were common (≈10%), clinically distinct, and often overlooked. They were linked to inotropes, transfusions, and cardiac dysfunction, with patterns differing by CABG versus valve surgery. These findings demand routine screening and targeted risk reduction in perioperative care.

Take-Home Message

Hallucinations after CABG and valve surgery are not rare, not benign, and not delirium. They affect 1 in 10 patients, arise from identifiable perioperative factors, and warrant systematic screening and tailored management to improve recovery and reduce distress.

Declaration

Competing Interests Statement

The authors declare that they have no known financial or personal relationships that could have appeared to influence the work reported in this paper. The authors declare no competing interests.

Availability of data statement

The datasets generated and analyzed during the current study are available from the corresponding author on reasonable request.

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Authors' contributions

Conceptualization, Methodology, Supervision, and Formal Analysis:
Haitham Abu Khadija, Nizar Abu Hamdeh, Duha Najajra, Wafiq Othman, Hamza A. Abdul-Hafez, Idiberto José Zotarelli Filho, Mohammad Alnees, Anwar Zahran

Writing – Original Draft:
Nizar Abu Hamdeh, Haitham Abu Khadija, Duha Najajra, Alaa Zayed

Writing – Review & Editing (Critical Revision of the Manuscript):
Alaa Zayed, Moaath Sawalha, Sara Ismail, Izzeddin Swidan, Omar Abu-Hamda, Oday Nana, Qassem Hamoudy, Basem Bali, Yahya Z. Fraitekh, Mohammad Masu'd, Mahdi Awwad

Investigation and Data Collection (across participating centers):
Moaath Nairat, Issa Al-Khdour, Ahmad Darwazah, Bisher Marzouqa, Mohammad Sbaih, Mustafa Shehadeh, Khalil Bali, Hasan Alkhatib, Helmi Tamimi, Ro'a Khalaf, Saja Karam, Aya Atatra, Ibraheem AbuAlrub, Raya Fuqha, Zahra'a Alhaj, Lila Abubilal, Wajeh Abuirmaileh, Mohammad Yasini, Alaa Dabash, Seleen Abu-Alhmam, Deema Mhesin, Saeed Bakeer, Yazan Hamdan, Osama Ewidat, Motasem Zahaika, Hanan Jboor, Abdalkarim Ali, Abdalfatah Badran, Kamal Issa, Abdelrahman Salous, Ghina Abukamleh, Merna Hazaza, Rou'a Farah, Rahaf Farah, Husam Abuzaina, Roua Najjar, Ameen Abu-Awad, Ayat Aljuba, Balqis Shawer, Omar Salah, Majd Shehadeh, Inas Jaber, Fatima Manassra, Doha Jaber, Batoul Jayouse, Yara Assaf, Ali Alrifai, Lourin Abuhaniah, Maya Altmaizee, Abdalaziz Darwish

Visualization (Figures, Forest Plots, Kaplan–Meier Curves):
Alaa Zayed, Moaath Sawalha, Idiberto José Zotarelli Filho

Project Administration:
Nizar Abu Hamdeh, Mohammad Alnees, Haitham Abu Khadija, Duha Najajra, **Hamza A. Abdul-Hafez, Abdalaziz Darwish, Omar Heih**

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Declaration of Competing Interests Statement

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Highlights

1. First Middle Eastern multicenter study on hallucinations after cardiac surgery
2. Hallucinations affected ~10% of CABG and valve surgery patients postoperatively
3. Risk factors included LVEF, cross-clamp time, transfusion, vasopressor use
4. Prolonged ventilation was paradoxically protective in valve surgery patients
5. Validated QPE tool ensured accurate detection of visual and auditory hallucinations