



# Intraoperative Awareness in Patients Undergoing Cardiac Surgery in an Academic Center in the North of Iran

Vali Imantalab<sup>1</sup>, Ali Mohammadzadeh Jouryabi <sup>1</sup>, Abbas Sedighinejad <sup>1</sup>, Mahboobeh Gholipour<sup>2</sup>, Leila Kanafi Vahed <sup>3</sup>, Seyed Sadegh Zargar-Nattaj<sup>4</sup>, Gelareh Biazar <sup>1,\*</sup> and Neda Shadkam<sup>5</sup>

<sup>1</sup>Department of Anesthesiology, Anesthesiology Research Center, Alzahra Hospital, Guilan University of Medical Sciences, Rasht, Iran

<sup>2</sup>Department of Cardiology, Cardiovascular Diseases Research Center, Heshmat Hospital, School of Medicine, Guilan University of Medical Sciences, Rasht, Iran

<sup>3</sup>Department of Community Medicine, Guilan University of Medical Sciences, Rasht, Iran

<sup>4</sup>Guilan University of Medical Sciences, Rasht, Iran

<sup>5</sup>Student Research Committee, School of Medicine, Guilan University of Medical Sciences, Rasht, Iran

\*Corresponding author: Department of Anesthesiology, Anesthesiology Research Center, Alzahra Hospital, Guilan University of Medical Sciences, Namjoo Street, P. O. Box: 4144654839, Rasht, Iran. Email: gelarehbiazar1386@gmail.com

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## Abstract

**Background:** Coronary artery bypass grafting (CABG) has distinctive characteristics that may increase the risk of awareness during general anesthesia (AGA).

**Objectives:** This study was conducted to assess the incidence of AGA in cardiac surgery in an academic hospital in Guilan, Iran.

**Methods:** This descriptive cross-sectional study was performed in Dr. Heshmat Hospital in Rasht, Iran. Eligible patients candidates for CABG were enrolled in the survey in 2022. After surgery, when the patient was cooperative enough, a questionnaire including demographic data and specialized questions related to different stages of anesthesia was completed via face-to-face interviews. The data were analyzed using IBM SPSS Statistics 21 with chi-square, Fisher's exact, and *t*-test.

**Results:** The data from 322 patients were analyzed, of whom 14 (4.3%) experienced AGA. Among them, the "feeling of fear and anxiety" reported by 9 (39.1%) cases was the most common awareness state. "Dreaming during surgery and anesthesia" and "feeling unable to move during anesthesia," each reported by 6 (26.1%) cases, were the other common types of awareness state. None of the demographic data had a significant association with the occurrence of AGA.

**Conclusions:** The incidence of AGA during CABG was almost acceptable according to the credible evidence.

**Keywords:** Intraoperative Awareness, General Anesthesia, Coronary Artery Bypass Grafting

## 1. Background

Awareness during general anesthesia (AGA) is a condition in which the patients can recall their surroundings or an event related to the surgery. It can be reported as pain, auditory perception, loss of motor function, helplessness, and panic. Awareness during general anesthesia is a significant concern for anesthesiologists and patients (1). According to individuals' conditions, anesthesiologists combine their clinical judgment with proper anesthetic agents and dosage to ensure that the patients are pain-free and in the appropriate depth of anesthesia during surgery. Despite the current effort, AGA remains unsolved, with unanswered aspects (2). Studies have demonstrated that advanced age, female gender, no use of opioid analgesics, tracheal intubation, and peri-operative anxiety were risk factors for AGA (3, 4). Studies have demonstrated that AGA can be associated with psychological complications, including

nightmares, lack of concentration, flashbacks, sleep disorders, post-traumatic stress disorder (PTSD), panic attacks, irritability, and even a tendency to avoid medical practice (5). Studies showed that using neuromuscular blocking agents and light anesthesia are the leading causes of awareness (6, 7). The overall incidence of AGA is reported as 0.1 - 0.2% (8) and 1.5 - 23% in coronary artery bypass grafting (CABG) patients. Hou et al. reported that cardiothoracic surgery was associated with the highest degrees of AGA (3). Generally, it is well established that there is a higher risk of AGA in cardiac surgery than in other surgical procedures. However, studies have shown a wide range of these complications, which can be affected by some factors.

The importance of the topic and the known side effects of awareness during surgery make it necessary to investigate the situation in an academic and referral heart surgery center in the province, which is the place of train-

ing for medical students and residents. However, to the best of our knowledge, medical literature is still rare in Iran, let alone in Guilan province.

## 2. Objectives

This study was planned to assess the incidence of AGA in cardiac surgery at Dr. Heshmat Hospital, the leading academic and unique center for cardiac surgeries in the North of Iran.

## 3. Methods

After the approval of the Research Ethics Committee of Guilan University of Medical Sciences (GUMS) and registration as ref: IR.GUMS.REC.1401.215, this descriptive cross-sectional study was conducted at Dr. Heshmat hospital in 2022. All study procedures complied with the ethical standards outlined in the Helsinki Declaration (2013).

### 3.1. Inclusion Criteria

We included patients over 18 years with exclusive coronary artery bypass surgery (not combined with valve surgery) under a cardiopulmonary bypass pump (CPB).

### 3.2. Exclusion Criteria

We excluded patients who were operated on under off-pump CABG, had severe and unexpected side effects changing the anesthesia or surgery method, were discharged before the visit, lacked proper cooperation, and were unable to interview.

In order to prevent the influence of the surgeon's expertise and surgical technique on the results, all surgeries were performed by a single cardiac surgeon. Regarding the anesthesia method, a standard protocol was performed in all patients. After the patient arrived at the operating room, standard monitoring, including pulse oximetry, end-tidal CO<sub>2</sub>, electrocardiography with leads II and V5 and automated ST-segment analysis, invasive arterial blood pressure, central venous pressure, and bispectral index (BIS) were started. Anesthesia was induced with midazolam 0.05 mg/kg, sufentanil 1 µg/kg, and propofol 1 mg/kg, and tracheal intubation was performed after the administration of cisatracurium 0.2 mg/kg. Anesthesia was maintained with continuous infusion of propofol 50 - 150 mg/kg/minute, sufentanil 0.1 - 0.3 µg/kg/hour, and cisatracurium 0.6 mg/kg/hour. After that, the patient underwent mechanical ventilation. During the operation, hemoglobin and hematocrit levels were kept above 9.5 and 25%, respectively; mean arterial blood pressure was maintained at 50 - 90 mmHg, arterial O<sub>2</sub> saturation above 95%,

BIS of 40 - 60, and end-tidal CO<sub>2</sub> of 35 - 40 mmHg. In order to achieve an activated coagulation time of more than 480 seconds, an initial dose of 300 u/kg heparin was administered, and then CPB was started. Cardiac arrest was induced by injecting a cold cardioplegic solution into the coronary arteries. During CPB, the mean blood pressure was kept at 50 - 70 mmHg, and hematocrit was maintained between 21% and 27%, with a body temperature of 32 - 34°C. The patients underwent median sternotomy, and the same standard technique of CABG surgery was considered for all of them. At the end of the surgery, protamine at a ratio of 1:1 was injected to fully reverse heparin effects.

After the vascular graft was complete and the patients had stable vital signs, they were disconnected from the heart-lung pump and transferred to the coronary care unit (CCU). At the end of the surgery, patients were transferred to the CCU to receive standard post-operation care. When standard clinical criteria were fulfilled, the weaning process was considered. When the patient was well cooperative, a direct interview was conducted to complete a questionnaire including demographic data (age, gender, BMI, education level, previous history of anesthesia, duration of surgery, duration of cardiopulmonary bypass, aortic clamp duration, and EF) and 14 specific questions about the last memory before anesthesia and the first memory after emergence from anesthesia and the status of AGA during anesthesia. This questionnaire was taken from the Arefian and Fathi study (9), and its content validity index (CVI) and content validity ratio (CVR) were assessed. For this purpose, 30 patients completed the questionnaire, and 10 expert faculty members of the Anesthesia Department reviewed the questions. The reliability of the questionnaire was calculated by Cronbach's alpha, and the content validity coefficient was 0.78.

### 3.3. Sample Size

Based on estimating the ratio of a qualitative trait (10), considering  $P = 0.23$ ,  $d = 0.046$ , and type I error of 5%, a minimum sample size of 322 cases was considered.

### 3.4. Statistical Analysis

IBM SPSS Statistics 21 software was applied to analyze the data with the chi-square test, Fisher's exact test, repeated measurements, and *t*-test. A *P*-value less than 0.05 was considered significant.

## 4. Results

During the study period, 385 patients were screened for eligibility: 45 did not meet the inclusion criteria, and 18 did not agree to participate for personal reasons. Finally,

the data from 322 cases were analyzed. The age range of the patients was 38 - 76 years, with a mean of  $58.45 \pm 6.8$  years, and 59.3% were male. The mean BMI was  $26.22 \pm 3.15$  kg/m<sup>2</sup>, the mean surgery time was  $209.56 \pm 40.28$  minutes, the mean aortic clamp time was  $29.72 \pm 6.77$  (15 - 45), and the mean cardiopulmonary bypass time was  $50.26 \pm 7.59$  (35 - 70). Most patients were ASA class II (65.8%) and had EF of more than 45% (56.2%). The demographic characteristics of the patients are summarized in [Table 1](#).

**Table 1.** Demographic Data of Patients Undergoing Coronary Artery Bypass Grafting Under General Anesthesia<sup>a</sup>

Variables	Values
<b>Gender</b>	
Male	191 (59.3)
Female	131 (40.7)
<b>Age (y)</b>	$58.45 \pm 6.8$ (38 - 76)
<b>Level of education</b>	
Illiterate	8 (2.5)
Elementary or middle school	62 (19.3)
High school	95 (29.5)
Diploma	110 (34.2)
University degree	47 (14.5)
<b>BMI (kg/m<sup>2</sup>)</b>	$26.22 \pm 3.15$ (18.73 - 34.89)
<b>ASA class</b>	
II	212 (65.8)
III	95 (29.5)
IV	15 (4.7)
<b>History of anesthesia and surgery</b>	
Yes	192 (59.6)
No	130 (40.4)
<b>EF</b>	
Less than 45%	141 (43.8)
More than 45%	181 (56.2)
<b>Aortic clamp time (min)</b>	$29.72 \pm 6.77$ (15 - 45)
<b>Cardiopulmonary bypass time (min)</b>	$50.26 \pm 7.59$ (35 - 70)
<b>Surgery time (min)</b>	$209.56 \pm 40.28$ (71 - 360)

<sup>a</sup> Values are expressed as No. (%) or mean  $\pm$  SD (range).

About the last event remembered before anesthesia induction, 94 (29.2%) of patients reported no recall, 61 (18.9%) reported anesthesiologist's general talks before being unconscious, and 41 (12.7%) of cases remembered the feeling of IV Insertion. Forty (12.4%) cases experienced the feeling of fear and anxiety about surgery as the last memory. About the first event that patients remembered immediately after emergence from anesthesia, 111 (34.5%) had no

recall, 75 (23.3%) had the sensation of the tracheal tube, 56 (17.4%) complained of feeling pain in the chest, and 20 (6.2%) of feeling thirsty, cold, or hot. The presence of a nurse at the bedside was also reported by 22 (6.8%). Hearing vague and incomprehensible noises around was another recalled event after emergence from anesthesia which was reported in 38 (11.8%) cases ([Table 2](#)).

**Table 2.** Frequency of the Last Memory Recalled Before Anesthesia and the First Memory After Emergence from Anesthesia

Memory	No. (%)
<b>The Last Memory Before Anesthesia</b>	
Anesthesiologist's general talks (Breathe deeply)	61 (18.9)
Drug injection by the anesthesiologist	14 (4.3)
IV insertion	41 (12.7)
Putting a face mask	36 (11.2)
Transferring to the operating room	25 (7.8)
Being present in the operating room	11 (3.4)
The feeling of fear and anxiety about surgery	40 (12.4)
I do not remember anything	94 (29.2)
<b>The First Memory After Emergence from Anesthesia</b>	
Feeling pain	56 (17.4)
The sensation of the tracheal tube	75 (23.3)
The presence of a nurse at the bedside	22 (6.8)
Feeling thirsty, cold, or hot	20 (6.2)
Hearing vague and incomprehensible noise	38 (11.8)
I do not remember anything	111 (34.5)

Besides, 14 (4.3%) of the enrolled patients experienced AGA. Among them, 23 cases of different awareness states were identified. "Feelings of fear and anxiety" was the most reported awareness in 9 (39.1%) cases. "Dreaming during surgery and anesthesia" and "feeling unable to move during anesthesia", each in 6 (26.1%) cases, were the other common types of awareness state. The frequency distribution of various awareness states is shown in [Table 3](#). In terms of demographic data, no significant difference was observed between patients who had experienced AGA and those who had not ( $P > 0.05$ ) ([Table 4](#)).

## 5. Discussion

There are different grades of AGA, from grade 0 (unconsciousness), indicating no recall and signs immediately or in more than 1 month, to grade 5 (consciousness), indicating explicit recall with distress, pain, and awareness with an emotional squeal ([11](#)). In this study, it seems that CABG patients experienced almost acceptable conditions before becoming unconscious. About the last event

**Table 3.** Frequency of Various Awareness States During General Anesthesia in Coronary Artery Bypass Grafting

A Variety of Awareness	No. (%)
Feeling unable to move during anesthesia	6 (26.1)
Hearing during anesthesia and surgery	0 (0)
Dreaming during anesthesia and surgery	6 (26.1)
Feelings of fear and anxiety	9 (39.1)
Feeling pain	2 (8.7)
Feeling the manipulation of the surgical area during anesthesia	0 (0)
Total	23 (100)

that was remembered before anesthesia, only 12.4% experienced fear of death and anxiety, which emphasizes the need for proper communication between the patient and the medical team involved, including nurses, anesthesiologists, and surgeons, in order to prevent peri-operative anxiety. However, regarding the first event remembered immediately after emergence from anesthesia, 46.9% experienced unpleasant conditions and complained of pain, tracheal tube sensation, inability to move, and feeling cold or hot. Obviously, the mentioned distressing situations could be appropriately managed. For example, effective interventions could be considered for primitive pain control before the emergence from anesthesia (12).

In this study, AGA was determined based on the patient's statements, which could not be considered as the limitation of this study. According to the current medical literature, there is no exact correlation between the findings of intraoperative monitoring and what was reported for AGA. Al-Husban et al. showed that based on the isolated forearm technique (IFT), the incidence of AGA was 40%, while none of these patients could remember any intra/peri-operative event (13). They concluded that anesthetic agents provide potent amnesia properties, even at sub-anesthetic doses (13). On the other hand, studies demonstrated that AGA merely detected based on technological monitoring did not result in significant psychological disorders when the patient had no recall (10, 14). Other studies have supported postoperative direct questioning instead of solely judgment on the monitoring (15). A recent review article emphasized that monitoring to detect the depth of anesthesia could not be equal to patients reporting AGA and was not routinely recommended (16). Zand et al. also found that the BIS was unreliable for detecting light anesthesia during surgery (17).

In another supporting study, Kunst et al. conducted a pilot trial on elderly cardiac surgical patients and investigated the effect of a combination of cerebral oxygenation monitoring, rScO<sub>2</sub>, and BIS on the depth of anesthesia (18).

They found that the depth of anesthesia improved in the intervention group; however, no significant difference was observed in cognitive function at 6 weeks between the intervention and control groups. They concluded that routine noninvasive anesthesia depth monitoring was feasible (18).

Although it seems the findings of this study, which were achieved by direct postoperative interviews, are reliable, a significant concern exists that it was difficult to distinguish between intra/peri-operative events and the emergence phenomena. Postoperative events, such as pain, and operating room voices, may be reported as AGA (1). Intraoperative dreaming, both pleasant and unpleasant, may also be related to light anesthesia or be part of emergence time (19).

Wang et al. investigated patients' AGA during cardiac surgery (20). The patients were interviewed 3 - 6 days after surgery, and any report on awareness was recorded. The AGA incidence in patients who underwent CABG under CPB, off-pump CABG, and septal repair or valve replacement under CPB was 4.7%, 9.6%, and 4%, respectively. Cardiopulmonary bypass pump did not significantly affect the incidence of AGA (20).

A systemic review on intraoperative awareness in cardiac surgery aimed to identify causes, predisposing factors, and squeals of AGA. It was concluded that the anesthesiologist's accuracy in identifying high-risk cases and using balanced anesthesia techniques reduced the occurrence of intraoperative awareness (21).

As mentioned, studies have reported contradictory results, which are justified by methodological differences, including inclusion criteria, studied populations, the time and the assessment tools, and the chosen type and dosage of anesthetics (22, 23). Certainly, the detection of AGA based on sympathetic systems activation symptoms such as lacrimation, sweating, tachycardia, and increased blood pressure is not as reliable as IFT (24), electroencephalogram (EEG) changes (25), or BIS (24, 26). In studies planned based on a direct interview, the questioning time is a determining factor. Therefore, a long time after surgery, the details of falling unconsciousness and emergence from anesthesia may not be wholly remembered. In addition, anesthetic agents differ according to the patient's medical conditions and co-morbidities, costs, and availability of drugs, which are all influencing factors (27-29). For example, during GA, propofol is associated with a higher incidence of AGA than isoflurane (30). Another study found that the administration of magnesium sulfate in GA was significantly associated with less postoperative pain and a higher depth of anesthesia (31). Obviously, AGA may not be completely avoidable; however, it could not be easily defended successfully. Therefore, it is recommended that the risk of

**Table 4.** Comparison of Demographic Data of Coronary Artery Bypass Grafting Patients with and Without Awareness During General Anesthesia <sup>a</sup>

Variables	Awareness During Anesthesia	No Awareness During Anesthesia	P-Value
<b>Gender</b>			0.2
Male	6 (3.1)	185 (96.9)	
Female	8 (6.1)	123 (93.9)	
<b>Age (y)</b>			0.521
≤ 50	3 (8.8)	31 (91.2)	
51 - 60	7 (4.1)	162 (95.9)	
61 - 70	4 (3.8)	100 (96.2)	
> 70	0 (0)	15 (100)	
<b>Mean ± SD</b>	58.42 ± 6.42	58.62 ± 6.81	0.915
<b>Education level</b>			0.153
Illiterate	0 (0)	8 (100)	
Elementary or middle school	0 (0)	62 (100)	
High school	5 (5.3)	90 (94.7)	
Diploma	5 (4.5)	105 (95.5)	
Academic degree	4 (8.5)	43 (91.5)	
<b>BMI (kg/m<sup>2</sup>)</b>	25.95 ± 2.81	26.23 ± 3.17	0.32
<b>ASA class</b>			0.303
II	11 (5.2)	201 (94.8)	
III or more	3 (2.7)	107 (97.3)	
<b>History of anesthesia and surgery</b>			0.846
Yes	8 (4.2)	184 (95.8)	
No	6 (4.6)	124 (95.4)	
<b>EF (percent)</b>	46.42 ± 5.34	46.44 ± 8.86	0.992
<b>Surgery time (min)</b>	207.14 ± 16.49	209.67 ± 41.04	0.625
<b>Cardiopulmonary pump time (min)</b>	49.28 ± 3.85	50.3 ± 7.71	0.488
<b>Aortic clamp time (min)</b>	29.64 ± 4.14	29.72 ± 6.87	0.761

<sup>a</sup> Values are expressed as No. (%) or mean ± SD.

AGA be discussed in high-risk patients undergoing cardiac surgery as one of the three high-risk surgeries for this event (8). Furthermore, when AGA occurs, and the patient declares some degree of awareness, denial worsens the situation, and the anesthesiologist might be sued. In contrast, it should be recorded in patients' medical documents, and a simple assurance and an apology would be effective (6, 32).

### 5.1. Conclusions

Awareness mainly occurs before bypass grafting or CPB in cardiac surgery. Most cases with awareness have auditory perceptions. Cardiopulmonary bypass pump is not the main factor affecting the incidence of CABG awareness. Surgical types do not affect the incidence of awareness of patients under CPB.

### 5.2. Limitations

Although valuable findings were found, we acknowledge a few limitations of this study. It was a single-center study, and patients with the experience of AGA were not followed to determine long-term psychological adverse consequences.

### Footnotes

**Authors' Contribution:** Study concept and design: V. I. and G. B.; drafting of the manuscript: A. M. and G. B.; acquisition of data: N. S. and A. S.; statistical analysis: N. S. and S. Z.; methodology: L. K.; analysis and interpretation of data: A. S. and M. G.; critical revision of the manuscript for impor-



tant intellectual content: All authors; study supervision: V. I. and A. M.

**Conflict of Interests:** The authors declare no conflict of interests.

**Data Reproducibility:** The data used and/or analyzed in the present study are available from the corresponding author upon reasonable request.

**Ethical Approval:** The study protocol was approved by the Research Ethics Committee of Guilan University of Medical Sciences and registered as (Ref: IR.GUMS.REC.1401.215).

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