Prevalence and risk factors of atrial fibrillation during lung and esophageal surgery
A Prospective observational study

Kangjie Xie, MD, a, b, Wen Zhang, MD, b, Jun Fang, MD, b, Ye Guo, MD, b, Man Fang, MD, b, Zewu Ding, MD, b, Yuqian Hu, MD, c, Weifeng Yu, PhD, d, Fugui Li, MD, e

Abstract
The aim of this prospective observational study was to screen for risk factors of intraoperative atrial fibrillation (AF) during noncardiac thoracic surgery. The study was conducted as a single-institution study in Zhejiang Cancer Hospital, Hangzhou, China. All the participants were patients with cancer scheduled for thoracotomy.

This study was conducted from July 2013 to August 2016 and included 144 patients scheduled for thoracotomy under general anesthesia. We collected the patients’ demographic and perioperative medical data in our hospital. AF was diagnosed using electrocardiography (ECG), on the basis of the presence of characteristic ECG features of AF by one or more ECG leads for at least 30 seconds.

Of the participants, 144 completed the study and 18 developed intraoperative AF. Higher percentages of subjects in the AF group than in the non-AF group had histories of chemotherapy (P = .014) and alcohol consumption (P = .034) before surgery. The AF group had a lower mean body mass index (P = .019), significantly higher mean heart rate (P < .001), and lower tidal volume (P = .01) than the non-AF group. After the logistic regression analysis, only alcohol consumption (odds ratio [OR] = 5.279; 95% confidence interval [CI]: 1.432–19.467), history of chemotherapy (OR = 4.019; 95% CI: 1.504–15.334), and high heart rate (OR = 1.093; 95% CI: 1.033–1.156) during 1-lung ventilation were identified as the risk factors of AF during lung and esophageal surgeries.

The incidence of intraoperative AF during noncardiac thoracic surgery was 12.5%. Alcohol consumption, history of chemotherapy, and high heart rate during 1-lung ventilation were the risk factors related to intraoperative AF.

Abbreviations: AF = atrial fibrillation, ASA = American Society of Anesthesiologists, BMI = body mass index, COPD = chronic obstructive pulmonary disease, CVP = central venous pressure, ECG = electrocardiography, FEV1 = forced expiratory volume in 1 second, FVC = forced vital capacity, HR = heart rate, MAP = mean arterial pressure, POAF = postoperative atrial fibrillation, RR = respiratory rate, VATS = video thoracoscopy-assisted thoracic surgery, VT = tidal volume.

Keywords: atrial fibrillation, chemotherapy, intraoperative, risk factor

1. Introduction
Perioperative cardiac arrhythmia, especially atrial fibrillation (AF), is much more common in noncardiac thoracic surgery than in general surgery. As reported, the incidence of AF varies widely from 9.9% to 19% in general thoracic surgery.[11-16] Even though it is a transient complication, it is related to longer hospital stays, greater clinical cost, increased stroke risk, and higher mortality rate.[11,14,17] Therefore, defining the risk factors for AF during general thoracic surgery and preventing the development of AF as much as possible are critical.

In previous studies, many risk factors were reported to be associated with the development of postoperative AF (POAF) such as older age, male sex, hypertension, obesity, smoking, alcohol consumption, and history of chronic obstructive pulmonary disease (COPD).[10,12] Furthermore, some surgical procedures are reported to be related to the occurrence of POAF.[13-16] Muranishi et al reported that mediastinal lymph dissection for patients with early-stage lung cancer is associated with a high risk for the development of POAF.[17] Lee et al reported that open thoracotomy was a more significant risk factor of POAF than video thoracoscopy-assisted thoracic surgery (VATS).[18] AF is a potentially preventable complication, as some risk factors such as smoking or surgical procedures are modifiable. We can evaluate the risk of surgical AF accurately and take actions to prevent the development of AF by defining more risk factors especially in surgical procedures.

A considerable proportion of patients received anti-tumor chemotherapy agents before thoracic surgery. However, whether patients who undergo chemotherapy are more prone to the development of AF than other patient populations during noncardiac thoracic surgery is still unknown. Several chemotherapy agents were reported to be related to cardiotoxicity.[18-22]
such as trastuzumab, 5-fluorouracil, and cisplatin. Neoadjuvant chemotherapy was reported to increase the risk of POAF after esophagectomy.\textsuperscript{[13]} Whether chemotherapy poses a risk factor for AF in general thoracic surgery needs further elucidation.

In addition, most patients developed AF during the first 3 days after surgery.\textsuperscript{[2,24]} Anesthesiologists are present in the operating and recovery rooms and are involved in the postoperative diagnosis and prophylaxis of this complication. However, almost all studies focused on the risk factors of POAF, not just intraoperative AF. The risk factors of intraoperative AF need to be further studied.

Therefore, we conducted this prospective study to identify more risk factors, including chemotherapy history in patients who underwent lung and esophageal surgeries, and further examine more risk-reducing measures.

2. Subjects and methods

2.1. Subjects

This prospective study was performed between July 2013 to August 2016 after receiving approval from the Human Research Ethics Board of Zhejiang Cancer Hospital (Ref: [2013]-06-98). The registered clinical trial number was ChiCTR-OCS-13003282. A written informed consent document was issued by each patient prior to participation.

The inclusion criteria were as follows: history of general thoracic surgeries for lung tumor, esophageal cancer, or mediastinal neoplasm; age ≥18 years; and normal liver and renal functions, acid and alkali balance, and electrolyte levels. The exclusion criteria included massive hemorrhage; histories of coronary heart disease, AF, ventricular arrhythmia, or other heart diseases; and previous lung or heart surgery before operation. In addition, patients with absolute and relative contraindications for surgery were excluded. Of the 180 patients recruited, only 144 completed the study. A flowchart of the study is presented in Flow Diagram.

![Flow Diagram](image)

2.2. Methods

On day 1, demographic data, including age, sex, body mass index (BMI), American Society of Anesthesiologists, smoking history, alcohol consumption, and chemotherapeutic agents, were collected. Medical history (hypertension, COPD, surgical, and medication history) was also recorded. Spirometry was administered preoperatively in accordance with the American Thoracic Society/European Respiratory Society guidelines.\textsuperscript{[23]} Results of the routine laboratory and arterial blood gas analysis were gathered. Then, each patient was requested to fast for solids and liquids at least 8 hours before surgery. No preoperative prophylaxis for AF was applied. Alcohol consumption was defined as consuming eight alcohol drinks or more per week for women and 15 or more per week for men.\textsuperscript{[9]}

On day 2, standard monitoring (electrocardiography [ECG], pulse oximetry, and invasive radial artery blood pressure) was established in the operating room. In almost all the patients, open thoracotomy was performed with general anesthesia combined with epidural anesthesia, except in those with a contraindication of epidural anesthesia. An epidural catheter was inserted between the T7-to-T8 or T8-to-T9 interspace before induction, and the placement of the catheter was confirmed by the administration of a 3-mL test dose of 1% lidocaine. The epidural catheter was left in situ for an average of about 3 days. In addition, the patients who underwent VATS simply received general anesthesia induced with midazolam (0.04 mg/kg), fentanyl (4 μg/kg), target-controlled infusion of propofol with plasma concentration (2.5–3.5 μg/mL), and rocuronium bromide (0.9 μg/kg). Then, orotracheal intubation was performed with a double-lumen endobronchial tube (Medtronic, Dublin, Ireland) or endobronchial blocker tube (COOPEDECH, Daiken Medical Co. Ltd, Osaka-ishi, Japan) after induction. The double-lumen tube or blocker position was confirmed using fiberoptic bronchoscopy. Anesthesia was maintained with a continuous infusion of remifentanil and target-controlled infusion of propofol to maintain the value of the bispectral index from 40 to 55, with or without sevoflurane. The intraoperative fluid (including lactated Ringer solution and hydroxyethyl starch) volume loading was performed at the discretion of the attending anesthesiologist. Data on heart rate, invasive blood pressure, arterial oxygen saturation, and ECG were recorded throughout the operation. Mechanical ventilation parameters were set by the attending anesthesiologist to maintain the PaCO2 between 35 and 45 mm Hg and were recorded.

After surgery, all the patients were transferred to the postanesthesia care unit and then transferred back to the ward after complete recovery. All the patients received continuous ECG and oxygen saturation monitoring for at least 72 hours after surgery. Data on 30-day mortality rates and length of hospital stay were also collected.

The AF was diagnosed using ECG on the basis of the presence of the characteristic ECG features of AF by one or more ECG leads for at least 30 seconds.\textsuperscript{[15]} Intraoperative AF was defined as new-onset AF during general thoracic surgery in patients with a normal ECG finding. Then, AF was managed and treated at the discretion of the attending anesthesiologist or surgeon in accordance with the latest guidelines.\textsuperscript{[13]}

2.3. Statistical analysis

The sample size was obtained using PASS (version 11, NCSS). As reported, the incidence of AF is approximately 19% in general thoracic surgery. A sample size of 124 was determined to be required for a power of 0.8 and an α value of 0.1. The SPSS version 22.0 software (SPSS Inc., New York) was used for statistical analysis. Normally distributed continuous data are expressed as mean ± standard deviation, while non-normally distributed data are presented as median (interquartile range
Table 1
Demographic characteristics of the subjects.

|                      | AF group, n=18 (%) | Non-AF group, n=126 (%) | P     |
|----------------------|--------------------|-------------------------|-------|
| Age, y               | 62.83 ±9.59        | 59.42 ±8.59             | .123  |
| >70                  | 4 (22.2)           | 10 (7.9)                | .137  |
| >60                  | 8 (44.4)           | 58 (46.0)               | .899  |
| Male/female          | 16 (88.9)/2 (11.1) | 95 (75.4)/31 (24.6)     | .330  |
| BMI, kg/m²           | 20.60 ±2.17        | 22.20 ±2.74             | .019  |
| Baseline heart rate  | 79.94 ±3.06        | 77.35 ±1.18             | .438  |
| Hypertension         | 3 (16.7)           | 17 (13.5)               | 1.00  |
| Diabetes mellitus    | 1 (5.6)            | 2 (1.6)                 | .825  |
| COPD                 | 1 (5.6)            | 5 (4.0)                 | 1.00  |
| History of any surgery | 4 (22.2)         | 34 (27.0)               | .886  |
| History of chemotherapy | 7 (38.9)        | 19 (15.1)               | .014  |
| Median smoking years (IQR) | 30.0 (40)     | 10.5 (40)               | .446  |
| Alcohol consumption  | 12 (66.7)          | 51 (40.5)               | .036  |
| ASA status           |                    |                        |       |
| I                    | 8 (44.4)           | 66 (52.4)               | .529  |
| II                   | 10 (55.6)          | 56 (44.4)               | .376  |
| III                  | 0                  | 4 (3.2)                 | 1.00  |
| Pulmonary function   |                    |                        |       |
| FEV₁, L             | 2.26±.29           | 2.35±.64                | .353  |
| FEV₁/FVC, %pred     | 88.13±16.45        | 85.14±17.54             | .535  |
| PVC, L              | 2.79±.37           | 2.77±.68                | .890  |
| FEV₁/FVC, %         | 82.03±11.28        | 84.77±9.81              | .321  |

Normally distributed continuous data were expressed as the mean±standard deviation; non-normally distributed data were expressed as median (IQR). AF=atrial fibrillation, ASA=American Society of Anesthesiologists status, BMI=body mass index, COPD=chronic obstructive pulmonary disease, FEV₁=forced expiratory volume in one second, PVC=forced vital capacity, IQR=interquartile range.

Table 2
Surgical and anesthetic differences between the AF and non-AF groups.

|                      | AF group, n=18 (%) | Non-AF group, n=126 (%) | P   |
|----------------------|--------------------|-------------------------|-----|
| Surgical method      |                    |                         |     |
| Thoracotomy          | 16 (88.9)          | 89 (70.6)               | .178|
| VATS                 | 2 (11.1)           | 37 (29.4)               |     |
| Surgical approach    |                    |                         |     |
| Right                | 12 (66.7)          | 91 (72.2)               | .625|
| Left                 | 6 (33.3)           | 35 (27.8)               |     |
| Chief surgeon        |                    |                         |     |
| Skilled (can perform complex thoracic surgery excellently) | 4 (22.2) | 52 (41.3) | .196|
| Unskilled (only can perform complex thoracic surgery independently) | 14 (77.8) | 74 (58.7) |     |
| Anesthetic way       |                    |                         |     |
| General anesthesia   | 5 (27.8)           | 47 (37.3)               | .431|
| Combined general-epidural | 13 (72.2)      | 79 (62.7)               |     |
| Endotracheal intubation |                |                         |     |
| Double lumen endobronchial tube | 3 (16.7)     | 17 (13.5)               | 1.00 |
| Bronchial occluder   | 15 (83.3)          | 109 (86.5)              |     |
| Operation duration, h | 4.1±1.4           | 3.5±1.4                 | .138 |
| Median crystal rehydration fluids, mL (IQR) | 2000 (600)     | 1700 (1000)             | .169 |
| Median colloid rehydration fluids, mL (IQR) | 750 (500)       | 1000 (500)              | .190 |
| Median blood loss, mL (IQR) | 200 (200)       | 200 (200)               | .603 |

Normally distributed continuous data were expressed as the mean±standard deviation; non-normally distributed data were expressed as median (IQR). AF=atrial fibrillation, IQR=interquartile range, VATS=video thoracoscopy-assisted thoracic surgery.

3. Results

3.1. Demographic characteristics of the subjects

Among the 144 patients, 18 developed AF during surgery while 126 did not. The commonly used chemotherapeutic agents by the patients included paclitaxel, fluorouracil, cisplatin, pemetrexed, gemcitabine, taxotere, and endostar (Table 1).

The AF group had higher percentages of subjects with histories of chemotherapy (P=0.014) and alcohol consumption (P=0.036) before surgery than the non-AF group. In addition, the AF group had a lower mean BMI than the non-AF group (P=0.019).

3.2. Surgical and anesthetic differences between the AF and non-AF groups

As shown in Table 2, no significant differences in surgical method (thoracotomy vs VATS), surgical approach (right vs left), type of operation, and skill of the chief surgeon were found between the 2 groups. No significant differences in anesthetic method (general vs combined general-epidural anesthesia) and endotracheal intubation (double-lumen endobronchial tube vs bronchial occluder) were demonstrated. Furthermore, no significant differences in surgical duration, crystal rehydration fluid volume, colloid rehydration fluid volume, and blood loss were found.

3.3. Differences in vital signs during surgery

Table 3 shows the vital signs during surgery. The average heart rate was significantly higher (P<.001) and tidal volume (<.05) was significantly lower in the AF group than the non-AF group, but no significant difference in tidal volume per kilogram was observed.
Postoperation incidence of intraoperative AF was 12.5%. Five of 18 patients
Heart rate during operation, beats/min 1.093 (1.033 – 1.156) .438
Median respiratory rate, breaths/min (IQR) 13.50 (3.00) .299
Median temperature, °C (IQR) 36.60 (0.50) .528
Median CVP, mm Hg (IQR) 8.00 (4.50) .909
During operation (1-lung ventilation)
Heart rate, beats/min 81.44 ± 15.33 .010
Median respiratory rate, breaths/min (IQR) 16.00 (2.00) .235
Median temperature, °C (IQR) 36.60 (0.50) .528
Median CVP, mm Hg (IQR) 8.00 (4.50) .909
Blood gas analysis
Median pH (IQR) 7.38 ± 0.06 .807
Median pO2, mm Hg (IQR) 209.00 (170.00) .838
Median pCO2, mm Hg (IQR) 43.00 (10.00) .339
Median respiratory rate, breaths/min (IQR) 13.00 (2.00) .299
Median tidal volume, mL (IQR) 475.00 (50.00) .010
V/weight, mL/kg 8.22 ± 0.75 .287
3.4. Binary logistic regression analysis
In the logistic regression analysis, alcohol consumption, history of chemotherapy, high heart rate, and tidal volume during one-lung ventilation were identified as risk factors of AF during surgery (Table 4).
3.5. Length of hospitalization
The length of hospitalization showed no significant difference between the AF and non-AF groups. Moreover, none of the patients died within 1 month after surgery.
4. Discussion
Studies published predominantly focused on perioperative AF, especially POAF. The present study focused on intraoperative AF. The major finding in the present study shows that the incidence of intraoperative AF was 12.5%. Five of 18 patients with POAF needed treatment in this study. AF was predominantly transient, did not affect hemodynamics or require clinical treatment. Furthermore, 41 patients had AF during the whole perioperative period, and the incidence was 28.5%, which is higher than those in previous studies.[2,9]
The present study also shows that alcohol consumption, history of chemotherapy, and high heart rate during 1-lung ventilation are risk factors of AF during surgery. Alcohol consumption was associated with AF, which was consistent with the finding of a prior study,[9] with the following possible reasons: alcohol consumption contributed to the exacerbation of systemic inflammatory response and cardiac insufficiency, which led to the increased susceptibility to AF,[24] and alcohol consumption might have caused autonomic dysfunction, which is a possible trigger for AF.[27]
We found that patients who underwent chemotherapy before surgery were more prone to develop intraoperative AF than other patient populations. The chemotherapy agents used included 5-fluorouracil, cisplatin, gemcitabine, and docetaxel, which were reported to be related to cardiotoxicity.[18–22] Cancer treatment may be associated with several cardiac events such as severe treatment-induced hypertension, vasospastic and thromboembolic ischemia, and rhythm disturbances, including QTc prolongation.[25,26] Chemotherapy might lead to structural and electrical remodeling of myocardial tissue. As reported, preexisting myocardial structural and electrical remodeling was associated with POAF.[19] Thus, we deduced that preoperative chemotherapy might cause intraoperative AF in patients who undergo noncardiac thoracic surgery.
In addition, we found that the average heart rate during 1-lung ventilation was much higher in the AF group than in the non-AF
group in the present study even though no significant difference in heart rate was found before surgery between the 2 groups. Furthermore, the average heart rate during operation was a risk factor of AF after the logistic regression analysis. Increased heart rate was reported to be associated with higher mortality in patients with AF.\textsuperscript{131} Several studies reported that preoperative use of oral beta-blockers prior to cardiac surgery may reduce the incidence of POAF\textsuperscript{52–54} and was recommended by several guidelines.\textsuperscript{15–37} As already known, beta-blockers could help control the heart rate and decrease the oxygen demand of the myocardium. However, our conclusion that increased heart rate during surgery is a risk factor of AF during noncardiac thoracic surgeries needs further study, as the occurrence of AF could lead to rapid ventricular rates, which might be a confounding factor. Thus, comparison of heart rates before the occurrence of AF during operation is required.

Moreover, the tidal volume in the AF group was smaller than that in the non-AF group. Lower tidal volume during 1-lung ventilation was a risk factor of intraoperative AF. As BMI was significantly higher in the non-AF group, the tidal volume was also highest in this group. Whether tidal volume is a risk factor remains to be clarified. Tidal volume was chosen on the basis of the absolute body weight. As no significant change in tidal volume was observed when normalized by weight, tidal volume is not a risk factor.

In the clinical work, we observed that unskilled (only can perform complex thoracic surgery independently) chief thoracic surgeons cause more intraoperative AF than skilled (perform complex thoracic surgery excellently), as show in my study, the incidence of POAF\textsuperscript{11}–\textsuperscript{16} was not analyzed because of the many contributing factors.

4.1. Limitations

A major limitation of the present study is that no long-term follow-up data were collected after surgery, so whether intraoperative AF is related to increased mortality is unknown. Furthermore, the small sample size might cover up the differences between the variables. In addition, no blood samples were collected, so it was quite difficult for us to examine the pathophysiology of AF. Recent studies reported that N-terminal pro-B-type natriuretic peptide and microRNA 483-5p levels are useful for identifying patients at risk.\textsuperscript{2,39,40}

Further studies are urgently needed to obtain more information and prevent the occurrence of AF.

5. Conclusion

The incidence of intraoperative AF during noncardiac thoracic surgery was 12.5%. Alcohol consumption, history of chemotherapy, and high heart rate during 1-lung ventilation were risk factors of intraoperative AF.

Author contributions

Conceptualization: Kangjie Xie, Ye Guo.

Data curation: Kangjie Xie, Ye Guo, Zewu Ding, Yuqian Hu.

Funding acquisition: Kangjie Xie.

Investigation: Man Fang.

Project administration: Kangjie Xie, Jun Fang, Weifeng Yu.

Resources: Jun Fang.

Software: Wen Zhang, Man Fang, Zewu Ding.

Supervision: Weifeng Yu.

Validation: Wen Zhang, Man Fang, Zewu Ding.

Visualization: Yuqian Hu.

Writing – original draft: Kangjie Xie, Wen Zhang.

Writing – review & editing: Kangjie Xie, Fugui Li.

References

\begin{itemize}
\item \textsuperscript{1} Vaporciyan AA, Correa AM, Rice DC, et al. Risk factors associated with atrial fibrillation after noncardiac thoracic surgery: analysis of 2588 patients. J Thorac Cardiovasc Surg 2004;127:779–86.
\item \textsuperscript{2} Cardinale D, Colomba A, Sandri MT, et al. Increased perioperative N-terminal pro-B-type natriuretic peptide levels predict atrial fibrillation after thoracic surgery for lung cancer. Circulation 2007;115: 1339–44.
\item \textsuperscript{3} Roselli EE, Murthy SC, Rice TW, et al. Atrial fibrillation complicating lung cancer resection. J Thorac Cardiovasc Surg 2005;130:438–44.
\item \textsuperscript{4} Onatmis M, D’Amico T, Zhao Y, et al. Risk factors for atrial fibrillation after lung cancer surgery: analysis of the Society of Thoracic Surgeons general thoracic surgery database. Ann Thorac Surg 2010;90:368–74.
\item \textsuperscript{5} Ivanovic J, Mazia D, Ramzan S, et al. Incidence, severity, and perioperative risk factors for atrial fibrillation following pulmonary resection. Interact Cardiovasc Thorac Surg 2014;18:340–6.
\item \textsuperscript{6} Imperatori A, Mariscalco G, Riganti G, et al. Atrial fibrillation after pulmonary lobectomy for lung cancer affects long-term survival in a prospective single-center study. J Cardiothorac Surg 2012;7:4–14.
\item \textsuperscript{7} Henri C, Giraldeau G, Dorais M, et al. Atrial fibrillation after pulmonary transplantation: incidence, impact on mortality, treatment effectiveness, and risk factors. Circ Arrhythm Electrophysiol 2012;5:61–7.
\item \textsuperscript{8} Nielsen TD, Bahnson T, Davis RD, et al. Atrial fibrillation after pulmonary transplant. Chest 2004;126:496–500.
\item \textsuperscript{9} Lee SH, Ahn HJ, Yeon SM, et al. Potentially modifiable risk factors for atrial fibrillation following lung resection surgery: a retrospective cohort study. Anaesthesia 2016;71:1424–30.
\item \textsuperscript{10} Hollings DD, Higgins RSD, Faber LP, et al. Age is a strong risk factor for atrial fibrillation after pulmonary lobectomy. Am J Surg 2010;199: 538–61.
\item \textsuperscript{11} Polanczyk CA, Goldman L, Marcantonio ER, et al. Supraventricular arrhythmia in patients having noncardiac surgery: clinical correlates and effect on length of stay. Ann Intern Med 1998;129:279–85.
\item \textsuperscript{12} Mitra N, Kuroda M, Miyoshi S, et al. Association of preoperative right and left ventricular diastolic dysfunction with postoperative atrial fibrillation in patients undergoing lung surgery: a prospective observational study. J Cardiothorac Vasc Anesth 2017;31:464–73.
\item \textsuperscript{13} Lee G, Wu H, Kalman JM, et al. Atrial fibrillation following lung transplantation: double but not single lung transplant is associated with long-term freedom from paroxysmal atrial fibrillation. Eur Heart J 2010;31:2774–82.
\item \textsuperscript{14} Tisdale JE, Wróblewski HA, Wall DS, et al. A randomized, controlled study of amiodarone for prevention of atrial fibrillation after thoracotomic esophagectomy. J Thorac Cardiov Surg 2010;140: 43–51.
\end{itemize}
Xie et al. Medicine (2018) 97:30

[15] Frendl G, Sodickson AC, Chung MK, et al. 2014 AATS guidelines for the prevention and management of perioperative atrial fibrillation and flutter for thoracic surgical procedures. Executive summary. J Thorac Cardiovasc Surg 2014;148:772–91.

[16] Gomez-Caro A, Moradillos FJ, Ausin P, et al. Risk factors for atrial fibrillation after thoracic surgery. Arch Bronconeumol 2006;42:9–13.

[17] Muranishi Y, Sonobe M, Menju T, et al. Atrial fibrillation after lung cancer surgery: incidence, severity, and risk factors. Surg Today 2017;47:232–8.

[18] Matos E, Jug B, Blagus R, et al. A prospective cohort study on cardio toxicity of adjuvant trastuzumab therapy in breast cancer patients. Arq Bras Cardiol 2016;107:40–7.

[19] Montella L, Caraglia M, Addo R, et al. Atrial fibrillation following chemotherapy for stage IIIIE diffuse large B-cell gastric lymphoma in a patient with myotonic dystrophy (Steinert’s disease). Ann Hematol 2005;84:192–3.

[20] Ferrari D, Carbone C, Codeca C, et al. Gemcitabine and atrial fibrillation. Eur J Cancer 2015;65:2523–5.

[21] Guglin M, Aljayeh M, Saiyad S, et al. Introducing a new entity: chemotherapy-induced arrhythmia. Europace 2009;11:1579–86.

[22] Ai D, Xu G, Feng L, et al. Dexmedetomidine does not reduce atrial fibrillation after lung cancer surgery. Eur J Cardio-Thorac Surg 2012;42:438–43.

[23] Arsenault KA, Yusuf AM, Crystal E, et al. Interventions for preventing post-operative atrial fibrillation in patients undergoing heart surgery. Cochrane Database Syst Rev 2013;31:CD003611.

[24] Ilarionov A, Hama S, Tsubokura M. Perioperative landiolol administration reduces atrial fibrillation after cardiac surgery: a meta-analysis of randomized controlled trials. Adv Ther 2014;31:440–50.

[25] Miller MR, Hankinson J, Brusasco V, et al. Standardisation of spirometry. Eur Respir J 2005;26:319–38.

[26] Samokhvalov AV, Irving HM, Rehm J. Alcohol consumption as a risk factor for atrial fibrillation: a systematic review and meta-analysis. Eur J Cardiovasc Prev Rehabil 2010;17:706–12.

[27] Larsson SC, Drca N, Wolk A. Alcohol consumption and risk of atrial fibrillation: a prospective study and dose-response meta-analysis. J Am Coll Cardiol 2014;64:281–9.

[28] Sutter TM, Ewer MS. Cancer drugs and the heart: importance and management. Eur Heart J 2013;34:1102–11.

[29] Nelson-Veniard M, Thambo JB. Chemotherapy-induced cardiotoxicity: incidence, diagnosis and prevention [in French]. Bull Cancer 2015;102:622–6.