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Short acting intravenous beta-blocker as a first line of treatment for atrial fibrillation after cardiac surgery: a prospective observational study

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KEYWORDS
Post-operative atrial fibrillation;
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Landiolol

Post-operative atrial fibrillation (POAF) defined as a new-onset of atrial fibrillation (AF) following surgery occurs frequently after cardiac surgery. For non-symptomatic patients, rate control strategy seems to be as effective as rhythm control one in surgical patients. Landiolol is a new highly cardio-selective beta-blocker agent with interesting pharmacological properties that may have some interest in this clinical situation. This is a prospective, monocentric, observational study. All consecutive adult patients (age >18 years old) admitted in the intensive care unit following cardiac surgery with a diagnosed episode of AF were eligible. Success of landiolol administration was defined by a definitive rate control from the beginning of infusion to the 72th h. We also evaluated rhythm control following landiolol infusion. Safety analysis was focused on haemodynamic, renal and respiratory side effects. From 1 January 2020 to 30 June 2021, we included 54 consecutive patients. A sustainable rate control was obtained for 49 patients (90.7%). Median time until a sustainable rate control was 4 h (1, 22). Median infusion rate of landiolol needed for a sustainable rate control was 10 µg/kg/min (6, 19). Following landiolol infusion, median time until pharmacological cardioversion was 24 h. During landiolol infusion, maintenance of mean arterial pressure target requires a concomitant very low dose of norepinephrine. We did not find any other side effects. Low dose of landiolol used for POAF treatment was effective and safe for a rapid and sustainable rate and rhythm control after cardiac surgery.

Introduction

Post-operative atrial fibrillation (POAF) is defined as a new-onset of atrial fibrillation (AF) following surgery and occurs frequently after cardiac surgery.[1,2] Aetiologies responsible for the occurrence of POAF are multifactorial.[6] The pathophysiological mechanisms triggering POAF are divided in two main chain of events: acute pathological disturbances related to surgical stress (i.e. inflammation, sympathetic activation and oxidative stress) resulting in an acute sinus node dysfunction and chronic alteration of the sinus node conduction related to myocardium remodeling occurring for example during ageing or myocardial ischaemic disease.[6–11] Almost 30% of patients are at risk of presenting a POAF event after cardiac surgery.[1,3] The onset of POAF depends partly on

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the type of surgery and occurs more frequently after valve replacement than coronary artery bypass grafting (CABG).[12-14] Patients presenting an episode of POAF are more frequently at risk of post-operative complications such as myocardial infarction, acute respiratory failure and stroke.[1,15] It has been reported that following cardiac surgery, POAF was also associated with an increase in health related costs, a prolonged intensive care unit (ICU) length of stay and a higher in-hospital mortality.[1,16] Following cardiac surgery, management of POAF represents a challenging issue, as it often occurs concurrently to haemodynamic instability related to post-operative period. Treatment strategies of POAF can be summarized by rate control or rhythm control strategies. Rate control strategy consists in decreasing heart rate to physiological values regardless the actual rhythm and rhythm control consist in restoring sinus rhythm. For non-symptomatic patients, rate control strategy seems to be as effective as the rhythm control one in surgical and medical patients.[3,4,17] Among the pharmacological option to treat POAF, infusion of very short acting beta-blocker seems a promising alternative.

Landiolol is a new highly cardio-selective beta-blocker agent with interesting pharmacological properties in cardiac surgery.[5] It has a very short acting half-life, a strong negative chronotropic action, low negative inotropic effect and poor vasoactive effect. Meta-analysis have pooled interventional studies investigated efficacy of landiolol for rhythm and rate control following cardiac surgery.[18,19] In a small randomized trial, infusion of landiolol was significantly more effective than diltiazem for rate and rhythm control, without any additional haemodynamic side effects.[20] Other studies reported that landiolol infusion efficiently prevented POAF compared to the standard of care after cardiac surgery.[21,22] Landiolol was also associated to a more effective rhythm control than amiodarone, with less cardiovascular side effects.[23] However, haemodynamic effect of landiolol should be better described as Wada *et al*.[24] demonstrated that hypotension was observed more frequently in patient with an altered LVEF. These results remain controversial as Sezai *et al*.[22] did not find any additional adverse event following low dose of landiolol infusion for patients with pre-existing cardiac dysfunction.

Therefore, there is a need of more knowledge on landiolol infusion side effects on haemodynamic, metabolic, renal and respiratory function in patient presenting a POAF event following cardiac surgery.

The aim of this study was to evaluate efficacy and safety of landiolol continuous administration in patients presenting POAF after cardiac surgery patients. Therefore, we studied the effect of continuous landiolol infusion following cardiac surgery on rate control and investigated specific side effects such as haemodynamic instability, respiratory failure, acute kidney injury (AKI) and metabolic disturbances.

Material and methods

Study design and population

The study is a prospective, monocentric, observational study. It was conducted in the eight-bed cardio-thoracic ICU of Brest Teaching Hospital. From 1 January 2020 to 30 June 2021, all consecutive adult patients (age >18 years old) admitted in the ICU following cardiac surgery and with a diagnosed episode of AF were eligible. All patients who received landiolol infusion for rate control according to our standardized practice (*Figure 1*) were included in this study. In our unit, landiolol infusion was considered as a first-line therapy for symptomatic AF and a therapeutic option for non-symptomatic AF (*Figure 1*). Symptomatic AF was defined by the presence of any of these clinical signs: pulmonary oedema, a 20% increase of norepinephrine infusion rate to maintain a predefined mean arterial pressure, a 15% decrease in cardiac index and/or a left ejection fraction <40% measured with echocardiography (*Figure 1*). For symptomatic and non-symptomatic AF, a rate control strategy was only considered if heart rate was above 110 b.p.m. We excluded patients with haemodynamic failure (defined by a norepinephrine infusion > 0.25 µg/kg/min and/or lactate level > 3 mmoL/L), a cardiogenic shock requiring inotrope drugs or a severe ARDS using the acknowledge definition.[25,26] We also excluded non-symptomatic patients who received oral beta-blocker for rate control. The current study was approved by the Ethics Committee of Brest Teaching Hospital in 2019 (registration number: B2019CE.05).

Protocolized landiolol administration

Landiolol starting infusion rate was set at 2 µg/kg/min. Then, infusion rate was progressively increased step by step (2 µg/kg/min) every 15 min to achieve the predefined heart rate goal. Success of the rate control was defined by a heart rate below 110 b.p.m.[4] For patients who achieved this goal, a bridge from landiolol to oral beta-blocker treatment was started, as soon as possible. After the first oral administration of beta-blocker, landiolol was progressively weaned by step of 2 µg/kg/min.

Data collection

In order to evaluate baseline characteristics, we prospectively collected several pre-operative variables such as: age, gender, weight, height, type of planned surgical procedure (CABG, valve replacement, other), valuable comorbidities (chronic kidney disease, cardiac insufficiency) and medication (beta-blockers, amiodarone, digoxin, diltiazem). From the beginning of the landiolol infusion to the 72th h, we prospectively recorded the following haemodynamic parameters: heart rate (b.p.m.), systolic arterial pressure (SAP, mmHg) and mean arterial pressure (MAP, mmHg). These haemodynamic parameters were collected at baseline, every 15 min until the 1st h, each hour until the 6th h, at the 8th h, at the 12th h and every 12 h until the 72th h. We also recorded every relevant treatment concomitantly administered such as: norepinephrine, amiodarone, oral beta-blockers and digoxin. The following biological parameters were collected: pH, lactate level (mmoL/L), creatinine level, urine output (mL/day), FiO_2 (fraction inspired oxygen) (%), SaO_2 (arterial saturation of oxygen) (%) and PaO_2 (arterial pressure of oxygen) (mmHg). For these

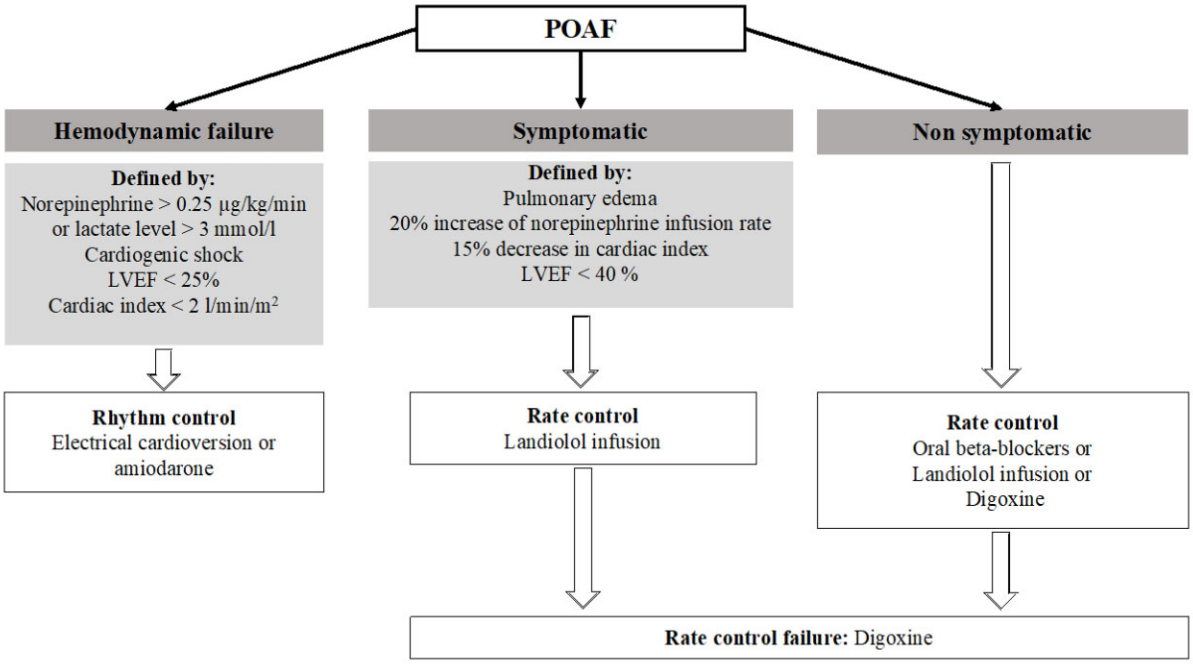

Figure 1 Study standardized management of post-operative atrial fibrillation.

parameters, the worst values were recorded at baseline and each day until the 72th h. Finally, we also collected every haemorrhagic and thromboembolic event during hospital stay.

Efficacy of landiolol infusion

Success of landiolol administration was defined by a definitive rate control from the beginning of infusion to the 72th h. We predefined a target of a HR below 110 b.p.m. for an appropriate rate control. Main efficacy outcome was predefined by the proportion of patients whose HR remained definitively below 110 b.p.m. in the 72 h after the beginning of landiolol infusion. We choose this target according to the European guidelines.[4] We also evaluated rhythm control by the proportion of pharmacological cardioversion following landiolol infusion as an exploratory efficacy outcome. To illustrate our results, we also calculated the median times (after the beginning of landiolol infusion) needed to obtain rate and rhythm control. Finally, we planned to identify any baseline characteristics associated with an early rate control.

Safety of landiolol infusion

First, we focused our safety analysis on haemodynamic effects following landiolol infusion. Severe haemodynamic side effects were collected, and haemodynamic instability related to landiolol infusion was predefined by: (i) a heart rate $<$ 50 b.p.m. and/or (ii) a SAP $<$ 90 mmHg or a MAP $<$ 50 mmHg despite an increase of infusion rate of norepinephrine $>$50%. Trend of all valuable haemodynamic parameters (such as heart rate, SAP, MAP) was described. We also described concomitant medication use, especially norepinephrine infusion, trend of oxygenation parameters (such as FiO_2, SaO_2 and $PaO_{2)}$ and metabolic disturbances (lactate level and creatinine level). For each patient, we also calculated an estimated glomerular filtration rate (eGFR) from baseline to Day 3. We focused this analysis on the proportion of patients who had an AKI (according to kidney disease improving global outcomes criteria) and/or had an elevated lactate level $>$2 mmoL/L.

Statistical analysis

Continuous variables were expressed as mean ($\pm$ SD) or median (interquartile range) if necessary. Categorical variables are expressed as percentage. To evaluate the trend in the main clinical parameters, continuous variables normally distributed were compared with paired Student's *t*-test and categorical variables were compared with χ^2 test. Finally, variables associated with an early and sustainable rate control (defined by a definitive HR $<$ 110 b.p.m. before the 4th h of landiolol infusion) were identified. For this univariate analysis, continuous variables normally distributed were compared with unpaired Student's *t*-test. A Wilcoxon test was used for other continuous variables. Categorical variables were compared with χ^2 test. For all analysis, statistical significance was set at $P < 0.10$. All statistical analysis was performed with R statistical software (version 3.6.0).

Results

Population

From 1 January 2020 to 30 June 2021, we included 54 consecutive patients who presented AF following cardiac

Table 1 Patients' characteristics before the onset of post-operative atrial fibrillation and efficacy outcome of landiolol infusion for rate control

	Overall $N = 54$
Baseline characteristics	
Age, years, mean (SD)	70 (7)
Gender, male, *n* (%)	44 (81.5)
Euroscore II, mean (SD)	4.8 (1.4)
NYHA	
Stage 1	23 (42.6)
Stage 2	24 (44.4)
Stage 3	7 (13)
Comorbidities, *n* (%)	
Cardiac insufficiency	3 (5.6)
Chronic kidney disease	6 (11.1)
Pre-existing AF	5 (11.1)
Surgery, *n* (%)	
CABG	36 (66.7)
Aortic valve replacement	23 (42.6)
Mitral valve replacement	5 (9.3)
Other	1 (1.9)
Respiratory support at baseline, *n* (%)	54 (100)
Invasive ventilation	9 (16.7)
Non-invasive ventilation	9 (16.7)
No mechanical ventilation	36 (66.7)
Medication at baseline, *n* (%)	
Norepinephrine	16 (30)
Amiodarone	5 (9.3)
Beta blockers	14 (25.9)
Onset of POAF after surgery, days, mean (SD)	2.4 (1.6)
Rate control during landiolol infusion	
Sustainable rate control (HR < 110 b.p.m.), *n* (%)	49 (90.7)
Time until sustainable rate control was achieved, h, median (IQR)	4 (1-22)
Infusion rate of landiolol, μg/kg/min, median (IQR)[a]	10 (6-19)

AF: atrial fibrillation; CABG: coronary artery by-pass grafting; POAF: post-operative atrial fibrillation.

[a]We reported infusion rate needed to obtain a sustainable rate control.

surgery. Surgical procedure was a CABG for 36 patients (66.7%), an aortic valve replacement for 23 patients (42.6%) and a mitral valve replacement for 5 patients (9.3%). At the onset of AF, 16 patients (29.6%) needed norepinephrine infusion and 14.9% of the patients presented hypoperfusion with a lactate level >2 mmoL/L. All relevant characteristics are summarized in *Table 1*.

Efficacy of landiolol infusion for rate and rhythm control

After the beginning of landiolol infusion, a sustainable rate control was obtained for 49 patients (90.7%). Median time until a sustainable rate control (HR <110 b.p.m. without relapse) was 4 h (1, 22) (*Figure 2A*). Landiolol infusion resulted in a significant decrease of heart rate 6 h (89 vs. 125 b.p.m.; $P < 0.001$) and 24 h after initiation of the infusion (76 vs. 125 b.p.m.; $P < 0.001$) compared to baseline (*Figure 3B*, *Table 2*). Median time until a temporary rate control (HR <110 b.p.m.) was achieve was 1 h (*Figure 2B*). Median infusion rate of landiolol needed for a sustainable rate control was 10 μg/kg/min (6, 19) (*Table 1*). Following landiolol infusion, median time until pharmacological cardioversion was 24 h (figure 2C). All valuable haemodynamic parameters were described on *Table 2* and *Figure 3*.

Safety of landiolol infusion

Except for heart rate and MAP, other haemodynamic parameters were comparable after the initiation of landiolol infusion (*Table 2*). In our cohort, the most frequent use of norepinephrine was observed at the 6th h following the start of landiolol infusion, when 30 patients (56%) needed norepinephrine (*Figure 3C*). At the 24th h, 22 patients (40.7%) needed norepinephrine infusion compared to the 16 patients (29.6%) who needed norepinephrine at baseline ($P < 0.001$) (*Table 2*, *Figure 3C*). For patients who needed norepinephrine, the mean norepinephrine infusion rate ranged from 0.04 to 0.11 μg/kg/min (*Figure 3C*). Paired analysis, which evaluates trends in terms of norepinephrine infusion rate, did not find any statistically significant differences over time (*Table 2*, *Figure 3C*). Landiolol infusion was stopped for haemodynamic instability in two patients (3.7%) after a median infusion time of 10 h (9-11). From baseline to Day 3, respiratory parameters were also comparable (*Table 2*). At Day 1, mean PaO_2/FiO_2 ratio was similar: 208 vs. 213; $P = 0.5$ (*Table 2*). Acid-base status was also comparable at Day 1. Interestingly, lactate levels were lower at Day 1 compare to the baseline value: 1.6 vs. 1.3 mmoL/L; $P = 0.009$ (*Table 2*). Finally, we did not observe any impairment in renal function from baseline to Day 3. Some relevant kidney function parameters (such as eGFR or urine output) were comparable or improved over time compared to baseline value (*Table 2*). As it was described on *Table 2*, the proportion of AKI patients decreased over time from initiation to Day 3. All relevant safety parameters were summarized in *Table 2*.

Variables associated with an early rate control

Univariate analysis did not identify any baseline variable associated with an early sustainable rate control (defined by a definitive HR < 110 b.p.m. before the 4th h of landiolol infusion).

We compared patients with early (≤4 h) rate control vs. patients with late (>4 h) or no rate control after starting landiolol infusion.

Pre-existing AF was more frequent in case of late or no rate control, but this difference was not statistically significant: 4.2 vs. 19%; $P = 0.27$. The Euroscore was comparable between the two groups: 4.9 vs. 4.6; $P = 0.56$. Neither use of amiodarone nor beta-blockers administration before landiolol infusion was associated with an early rate control. Furthermore, proportion of patients who needed norepinephrine before landiolol infusion was similar between the two groups: 31 vs. 28%; $P = 1$. At initiation of landiolol infusion, rate of infusion was

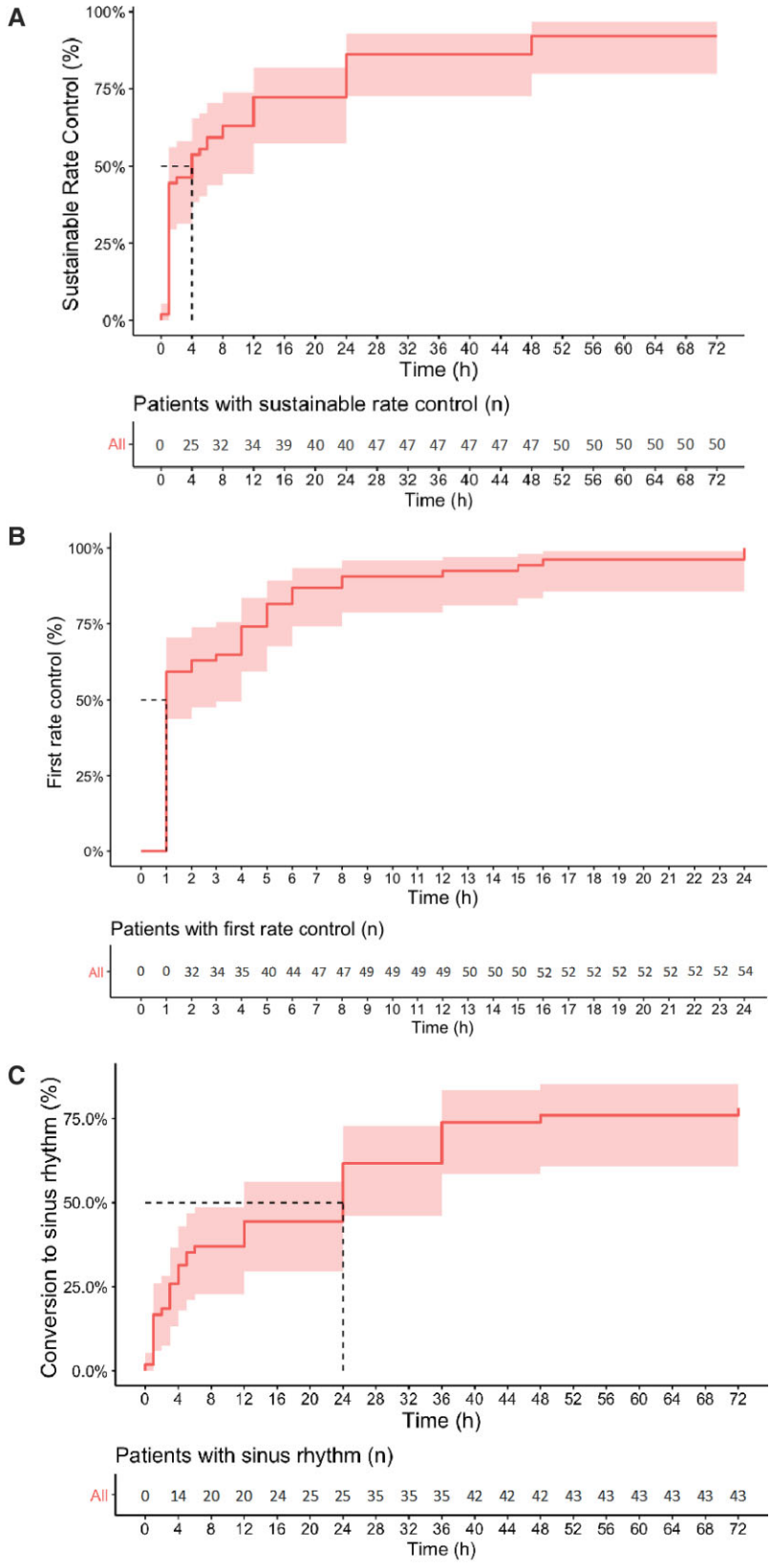

Figure 2 Percentage of rate and rhythm control during landiolol infusion from the initiation to the 72th h. (*A*) Proportion and number of patients with a sustainable rate control. (*B*) Proportion and number of patients with first rate control. (*C*) Proportion and number of patients with conversion to sinus rhythm.

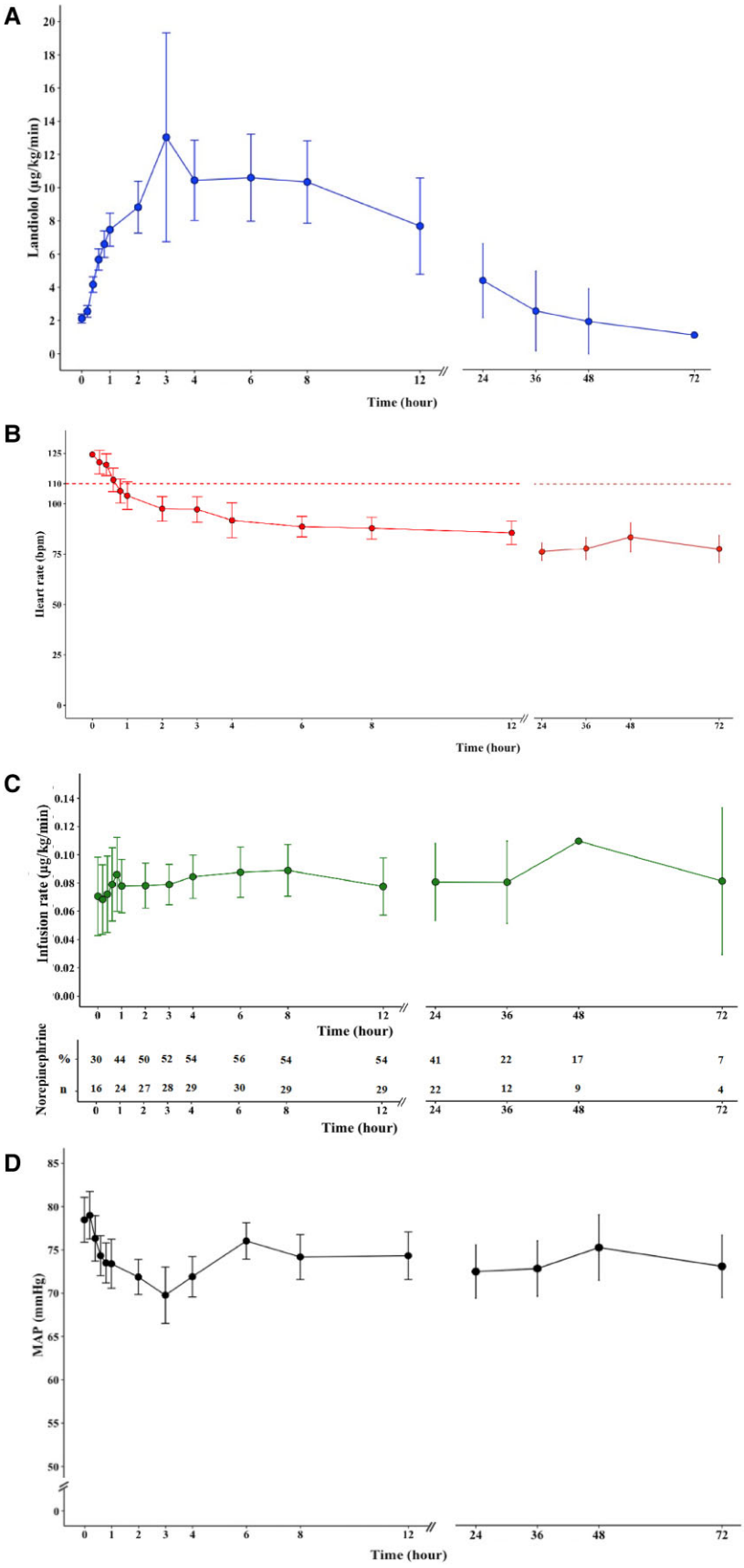

Figure 3 Trend of the main haemodynamic parameters. We reported mean values and confidence interval (CI 95%) from the beginning of landiolol infusion to the 72th h. (*A*) Mean landiolol infusion rate (µg/kg/min) over time. (*B*) Heart rate (b.p.m.) changes over time. (*C*) Mean norepinephrine infusion rate (µg/kg/min), number/proportion of patients who needed norepinephrine over time. (*D*) Mean arterial pressure (mmHg) changes over time.

Table 2 Tolerance of landiolol infusion from initiation of treatment to Day 3. From Day 1 to Day 3, worst values per day for each parameters are reported

	Landiolol initiation	Day 1	Day 2	Day 3
Haemodynamic parameters				
HR (b.p.m.), mean (SD)	125 (23)	76 (15)*	83 (21)*	78 (18)*
SAP (mmHg), mean (SD)	116 (15)	116 (16)	116 (16)	120 (13)
MAP (mmHg), mean (SD)	79 (10)	75 (10)*	77 (10)	75 (8)*
Norepinephrine infusion, *n* (%)	16 (29.6)	22 (40.7)*	9 (16.7)	4 (7.4)
Infusion rate (μg/kg/min), mean (SD)	0.07 (0.05)	0.08 (0.06)	0.11 (0.07)	0.08 (0.03)
Respiratory parameters				
PaO_2 (mmHg), mean (SD)	96 (34)	94 (25)	92 (17)	86 (16)**
SpO_2 (%), mean (SD)	96 (4.6)	97 (2.1)**	97 (2.7)**	97 (2.7)**
PaO_2/FiO_2, mean (SD)	208 (88)	213 (97)	205 (83)	206 (70)
FiO_2 (%), mean (SD)	49 (13)	48 (14)*	48 (15)*	44 (8.7)*
Acid base status				
pH, mean (SD)	7.42 (0.04)	7.41 (0.05)*	7.44 (0.04)*	7.44 (0.04)
Lactate level (mmoL/L), mean (SD)	1.6 (0.9)	1.3 (0.5)*	1.2 (0.4)*	1.1 (0.4)*
Lactate level > 2 mmoL/L, *n* (%)	2 (3.7)	2 (3.7)	2 (3.7)	1 (1.85)
Renal function				
AKI, *n* (%)	7 (13)	3 (5.6)*	3 (5.6)*	1 (1.9)*
Stage 1	0	0	0	1 (1.9)
Stage 2	4 (7.4)	3 (5.6)	2 (3.7)	0
Stage 3	3 (5.6)	0	1 (1.9)	0
eGFR (mL/kg/1.73 m^2), mean (SD)	82.3 (36)	86.4 (35)**	90.4 (33)*	89 (32)*

Tests performed were paired Student's *t*-test for continuous variables and χ^2 test for categorical variables. Significance levels were as follows: *$P < 0.05$; **$P < 0.10$. Variables were compared to landiolol infusion initiation.

AKI: acute kidney injury; eGFR: estimated glomerular filtration rate; HR: heart rate; IQR: interquartile range; MAP: mean arterial pressure; SAP: systolic arterial pressure; SpO_2: peripheral capillary oxygen saturation.

similar between the two groups (2.2 vs. 2.1 μg/kg/min; $P = 0.78$). Median length of landiolol infusion was longer in case of late or no rate control: 8 vs. 12 h; $P = 0.001$. During landiolol infusion, amiodarone was more frequently administered in case of a late or no rate control: 6.9 vs. 28%; $P = 0.09$. In case of early sustainable rate control, no thromboembolic event was recorded compared to the two events identified in case of a late or no rate control, but this difference was not statistically significant ($P = 0.41$). Median ICU length of stay was significantly reduced in case of an early rate control: 5 vs. 7 days; $P = 0.005$.

Discussion

In this observational study, a sustainable rate control was rapidly obtained following landiolol infusion with a median time of 4 h and a median infusion rate of 10 μg/kg/min. Concomitantly, to achieve arterial pressure target, infusion of a very low dose of norepinephrine was required in 56% of patients. In our study, no significant adverse event was identified in the first 72 h following landiolol infusion.

Optimal treatment for the management of POAF following cardiac surgery remains unclear.[4] For rate control strategy, beta-blockers remain an interesting therapeutic during the post-operative period.[4] Khan *et al.*[27] reported that beta-blockers, when it was administered preoperatively, can prevent efficiently POAF after cardiac surgery. However, in this report almost 20% of the patients presented POAF despite preoperative oral prophylaxis.[27] Failure to prevent PAOF could be explained by a compromised bioavailability of oral beta-blockers immediately after cardiac surgery due to gastroparesis.[28] Therefore, development and evaluation of new intravenous beta-blockers remains a promising perspective in this context. Currently, there are only two intravenous short-acting beta-blockers available: esmolol and landiolol.[29] Landiolol is a new highly cardioselective, ultra-short acting beta-blocker. Compared to the existing drugs (such as esmolol), landiolol has some interesting pharmacological properties, which are potentially helpful in the context of cardiac surgery: shorter half-life (4 min), low negative inotropic effect, less hypotensive effect and more effective negative chronotropic effect.[5] In two small monocentric randomized trial, Sezai *et al.*[21,22] demonstrated that POAF was reduced with low-dose of landiolol when initiated at the time of vascular anastomosis during CABG. Even for patients presenting a pre-existing cardiac dysfunction, there was no related haemodynamic side effects to landiolol infusion.[21,22] However, there are only few available studies which evaluated landiolol administration as first-line treatment for rate control in patients with POAF following cardiac surgery.[30,31] In a case-control study, rate and rhythm control were more frequently obtained with landiolol after CABG.[31] In this cohort, some factors which were associated to a negative response to landiolol were identified: urgent surgery and use of other

antiarrhythmic.[31] In our study, we did not identify any clinical characteristics (except pre-existing AF) which affect landiolol efficacy. Unfortunately, the authors did not evaluate the consequences of treatment failure on clinical outcome.[31] However, an early (in 4 h) and sustainable rate control was associated with a reduced ICU length of stay in our study. In another observational study, sinus rhythm was more frequently restored with landiolol compared to the use of amiodarone.[23] In this study, Shibata *et al*.[23] excluded patients who received additional treatment with landiolol infusion which introduced a selection bias: the more severe AF cases who needed concomitant therapy might be excluded. The results of these two studies[23,31] were limited by important bias due to the retrospective non-randomized design of the study. In addition, evaluation of safety profile of landiolol cannot be reliably evaluated on data collected retrospectively. In a randomized controlled study, Sakamoto *et al*.[30] demonstrated a better efficacy of landiolol infusion compared to diltiazem in regards to conversion to sinus rhythm. In this study, rate controlled was obtained in 97.1% of patients.[30] Considering efficacy of landiolol on rate control, our results are in line with these findings. The results of the randomized controlled trials (RCTs) were summarized in two meta-analysis, which underlined some important limitations: open-label evaluation of the outcomes, small sample size and mono-centre studies.[18,20] Despite these limitations, all these studies did not find any additional haemodynamic side effects linked to the use of landiolol.[23,30,31]

Compared to the already published articles, the current study provides some additional and precise information on haemodynamic status immediately after landiolol infusion and during the first 72 h.[30,31] To our knowledge, our study is the first one reporting proportion of patients who needed a concomitant norepinephrine infusion to achieve MAP target. However, infusion rate of norepinephrine required to maintain blood pressure were extremely low. Moreover, we cannot rule out that norepinephrine requirement was also due to vasoplegia following cardiac surgery. Moreover, a meta-analysis underlined that some important outcomes such as ICU length of stay were not recorded in recent RCTs.[20] In our study, patients who had an early and sustainable rate controlled had a significant reduction in ICU length of stay. Moreover, our study provides some other information about safety profile of landiolol infusion on respiratory and renal function.

The current study has some strength and limitations. Regarding strength, all data were prospectively collected, and all expected side effects were pre-defined making this study the first prospective one in the field. Moreover, all eligible and consecutive patients were included in our cohort, and all type of cardiac surgeries were considered. Therefore, we believe that selection and evaluation bias were minimized compared to other studies. To our knowledge, we also report the first observational study which prospectively evaluated efficacy of landiolol for rate control strategy after cardiac surgery.

However, our study has some limitations. Firstly, it is a single-centre observational prospective study on current practice in a cardiothoracic ICU. Therefore, there is no comparison of the observed cohort to a control one in our study. This limit the conclusion of our study to efficacy and safety of the treatment used in the protocol. Other studies will be required to assess the potential superiority to other anti-arrhythmic drug currently available. Finally, almost 30% of the patients in this study, received beta-blocker and/or amiodarone before landiolol infusion initiation. This bias has been a caveat in several other studies.[23,30,31]

Conclusion

In our study, low dose of landiolol used for POAF treatment was effective for a rapid and sustainable rate and rhythm control after cardiac surgery. An early and sustainable rate control was also associated with reduction of median ICU length of stay. Except for the requirement of concomitant low-dose of norepinephrine to maintain blood pressure, we did not find any other side effect following landiolol infusion. Our results suggest that landiolol could be safely used as first-line therapy for rate control in a safe environment such as high dependency units or ICU. Further large prospective randomized controlled study should be performed to compare landiolol with other beta-blocker and/or anti-arrhythmic treatment to confirm our findings.

Conflict of interest: O.H.: consultancy fees for AMOMED; J.F.O.: Consultancy fees and lecture for Amomed.

Data availability

Data are available on demand to corresponding author.

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