Purpose: Atrial fibrillation (AF) is the most common arrhythmia treated in the world. While medical treatment with antiarrhythmic drugs remains the primary treatment modality, symptomatic refractory AF often requires treatment with a catheter or surgical ablation. One minimally invasive therapy is the Mini-Maze procedure, which utilizes epicardial radiofrequency ablation via a subxiphoid approach to rid the heart of arrhythmogenic atrial foci without a median sternotomy or cardiopulmonary bypass. The goal of this retrospective cohort study was to identify clinical factors associated with metabolic acidosis following the Mini-Maze procedure.

Materials and Methods: After Institutional Review Board approval, we studied patients undergoing the Mini-Maze procedure, off-pump coronary artery bypass grafting or patients conventional Cox-Maze on cardiopulmonary bypass. The first base deficit value obtained in the Intensive Care Unit was used as a measure of metabolic acidosis. Using logistic regression with Akaike information criteria, we analyzed preoperative, intraoperative, and postoperative data to determine the factors associated with changes in base deficit.

Results: A multivariable model using stepwise selection demonstrated that diabetes mellitus and weight were associated with a decrease in the base deficit by 2.87 mEq/L (95% CI: −5.55–−0.19) and 0.04 mEq/L (95% CI: −0.08, 0.004), respectively. Furthermore, creatinine was associated with a 1.57 mEq/L (95% CI: 0.14, 2.99) increase in the base deficit.

Conclusion: The Mini-Maze procedure was not associated with postoperative metabolic acidosis. Instead, nondiabetic patients and patients with higher creatinine were associated with greater base deficits after undergoing cardiac surgery.

Key words: Cardiac surgery; Metabolic acidosis; Minimally invasive surgery; Radiofrequency maze procedure; Retrospective study

INTRODUCTION

Atrial fibrillation (AF) is the most common arrhythmia treated in the world with an estimated prevalence of 33.5 million in 2010.[1] Although medical management of AF using a class one antiarrhythmic remains the first line of treatment,[2,3] symptomatic refractory AF often requires treatment with a catheter or surgical ablation. There are multiple evolved and evolving catheter-based surgical treatment strategies.[4,5] One minimally invasive therapy is the Mini-Maze procedure that utilizes epicardial radiofrequency ablation via a subxiphoid approach to rid the heart of arrhythmogenic atrial foci.[4,5] Based on advances in minimally invasive cardiac surgery, this procedure is performed without a median sternotomy or cardiopulmonary bypass.[6,7]

At the University of Michigan Cardiovascular Center, we have performed 12 Mini-Maze
procedures using the subxiphoid exposure. This surgery requires single lung ventilation and retraction of surrounding soft tissue structures to access the pulmonary veins as the left atrium is isolated; this facilitates the exposure of the arrhythmogenic pathways for optimal radiofrequency ablation. However, this maneuver may put the patient at risk for prolonged hypotension, malperfusion, and tissue ischemia. The metabolic consequences of this novel approach remain largely unknown. While there are numerous etiologies for metabolic acidosis, it occurs primarily as a consequence of excess lactic acid or ketoacid production relative to inadequate consumption, renal acid excretion, and bicarbonate formation. Severe acidemia can lead to serious cardiovascular and neurologic compromise, including death. Even small increases in lactic acid are suggestive of organ ischemia and are associated with longer Intensive Care Unit (ICU) stays and increased morbidity.[8] The purpose of this study is to determine if there is an association between metabolic acidosis and Mini-Maze. Understanding the factors that contribute to metabolic acidosis in Mini-Maze patients may help to prevent metabolic acidosis and its putative complications in these patients.

MATERIALS AND METHODS

After obtaining Institutional Review Board approval, which waived informed consent, a retrospective chart review was performed of 36 cardiac surgical patients. Twelve patients underwent the minimally invasive MAZE (Mini-Maze) procedure without cardiopulmonary bypass. To provide a contextual basis for analysis, two control groups were examined, which included 12 patients who underwent off-pump coronary artery bypass surgery (OPCAB) and 12 patients who underwent conventional isolated Cox-Maze with cardiopulmonary bypass. We chose these two control groups as the conventional Cox-Maze procedure is similar to the Mini-Maze in the type and extent of direct cardiac injury from the ablation while the OPCAB group is similar to the Mini-Maze procedure in mechanically restricting and stabilizing the heart, while avoiding cardiopulmonary bypass. Data were collected querying the electronic medical record (EMR) (Centricity, General Electric Healthcare, Waukesha, WI).

All three patient groups consisted of the last 12 consecutive patients to undergo each of the three procedures. The Mini-Maze surgeries were performed by one surgeon. The control group procedures were performed by any of six cardiac surgeons. All Mini-Maze patients underwent a subxiphoid surgical approach and received the standard anesthetic for cardiac procedures at our institution employing induction with fentanyl, 10–15 µg/kg, midazolam, 0.1 mg/kg, supplemented by propofol, isoflurane maintenance, and muscle relaxation with vecuronium. In addition, a double-lumen endotracheal tube was placed in all Mini-Maze patients for single-lung ventilation to facilitate exposure of the pulmonary veins. Alternatively, all non-Mini-Maze patients underwent conventional median sternotomy and received the previously mentioned standard cardiac anesthetic with a single lumen endotracheal tube. Intraoperatively, an insulin infusion, if needed, was used on all patients to keep glucose <150 mg/dL. A propofol infusion, 2–6 mg/kg/h, was used to sedate patients postoperatively for transport to the ICU until extubation criteria were met. Patients who were extubated on the day of surgery were given neostigmine and glycopyrrolate for reversal of neuromuscular blockade. All patients had postoperative blood drawn upon arrival in the ICU, including arterial blood gas, which contained the base deficit level. Patient demographics and hemodynamic data were collected, and intraoperative vital signs were grouped into 10-min intervals or epochs during which hemodynamic parameters were analyzed. The median number and range of these threshold events for each subject were tabulated and compared.

The base deficit level measured immediately after arrival in the ICU after surgery was used to quantify the level of postoperative metabolic acidosis. To determine differences between the three groups, we first conducted univariate analyses with Kruskal–Wallis tests for continuous data and Fisher-exact tests for categorical data, then univariate linear regression to determine the amount of base deficit associated with each factor. Next, multivariable linear regressions using all factors with univariate \( P < 0.2 \) and preoperative bicarbonate levels were created. Models were explored by hierarchically excluding diabetes and its interaction. The final model was created using step-wise selection with the inclusion of factors that minimized the Akaike information criterion. All statistics were done in R version 3.0.2 (R Foundation, Vienna, Austria).[9]

RESULTS

Patients in all three groups had similar demographic characteristics and preoperative laboratory values,
but OPCAB patients were more likely to have diabetes mellitus treated with insulin and a recent myocardial infarction [Table 1]. Operative risk calculated from EuroScore II was similar amongst the groups [Table 1] and there were no deaths in any group. They also exhibited similar intraoperative hemodynamics [Table 1]. Patients who underwent the Mini-Maze procedure had similar postoperative base deficits = 4.6 mEq/L (2.5–6.3) (median [interquartile range]) compared to patients undergoing OPCAB 4.1 (1.4–5.6) and conventional maze 1.5 (1.0–2.5), \( P = 0.203 \), and similar postoperative bicarbonate levels: 22 mEq/L (19.4–24.0), 20.65 (19.9–23.0), and 22.95 (21.9–23.4), \( P = 0.280 \); respectively. However, the type of surgical

| Table 1: Patient demographics, laboratory values, and hemodynamic parameters |
|-----------------|-----------------|-----------------|
| Factor          | Mini-Maze \( n (\%) \) | OPCAB \( n (\%) \) | Conventional Maze \( n (\%) \) |
| Female          | 2 (17)          | 4 (33)          | 6 (50)          | 0.283 |
| Diabetes mellitus on insulin | 0 (0)          | 4 (33)          | 1 (8)           | 0.038 |
| Peripheral vascular disease | 1 (8)          | 0 (0)          | 0 (0)           | 0.999 |
| Chronic lung disease | 0 (0)          | 1 (8)          | 0 (0)           | 0.999 |
| Recent myocardial disease | 0 (0)          | 4 (33)          | 0 (0)           | 0.008 |
| Renal failure   | 1 (8)           | 0 (0)          | 0 (0)           | 0.999 |

| Factor          | Median | IQR  | Median | IQR  | Median | IQR  |
|-----------------|--------|------|--------|------|--------|------|
| Age (years)     | 62     | 55-65| 65     | 60-68| 68     | 61-79| 0.374 |
| ASA class       | 3      | 3-3  | 4      | 4-4  | 3      | 3-4  | 0.108 |
| Height (cm)     | 183    | 178-188| 172   | 161-181| 168   | 165-179| 0.665 |
| Weight (kg)     | 110    | 101-119| 84    | 78-104| 87.6   | 73-101| 0.468 |
| BMI (kg/m²)     | 33     | 31-35| 30     | 26-35| 30     | 25-33| 0.468 |
| Ejection fraction | 0.60   | 0.54-0.60 | 0.55   | 0.55-0.56| 0.60   | 0.54-0.61| 0.796 |
| Preoperative creatinine (mg/dL) | 1.0   | 0.8-1.1| 1.0   | 0.8-1.2| 1.1   | 1.1-1.2| 0.612 |
| Preoperative hematocrit (%) | 43.0  | 40.4-46.6| 40.2  | 35.6-43.8| 42.4  | 40.8-44.5| 0.535 |
| Postoperative base deficit (mEq/L) | 4.6   | 2.5-7.1| 4.1   | 1.2-5.8| 1.5   | 0.9-2.5| 0.191 |
| Preoperative bicarbonate (mEq/L) | 29.5  | 27.5-30.5| 27    | 25-28| 29     | 26.5-31| 0.298 |
| Euroscore II    | 1.15   | 0.72-1.41| 1.54  | 1.16-2.53| 2.47  | 1.58-5.70| 0.796 |
| Case duration (min) | 141  | 131-172| 238   | 203-300| 225   | 199-245| 0.353 |
| #epoch MAP <50 mmHg (in-room to surgical start) | 0   | 0-0  | 0      | 0-0  | 0      | 0-0  | 1.000 |
| #epoch MAP <60 mmHg (in-room to surgical start) | 0   | 0-1  | 0      | 0-2  | 0      | 0-0  | 0.848 |
| #epoch MAP <70 mmHg (in-room to surgical start) | 3   | 2-5  | 5      | 3-6  | 2.5   | 1-3  | 0.057 |
| #epoch MAP <50 mmHg (surgical start to end) | 1   | 0-5  | 0      | 0-5  | 1      | 0-1  | 0.320 |
| #epoch MAP <60 mmHg (surgical start to end) | 3   | 0-19 | 8.5    | 6-17 | 4      | 3-7  | 0.183 |
| #epoch MAP <70 mmHg (surgical start to end) | 22  | 10-35| 49.5   | 36-57| 14     | 13-18| 0.364 |
| #epoch MAP <50 mmHg (in-room to surgical end) | 1   | 0-5  | 0      | 0-5  | 1      | 0-1  | 0.285 |
| #epoch MAP <60 mmHg (in-room to surgical end) | 3   | 0-19 | 8.5    | 6-17 | 4      | 3-7  | 0.183 |
| #epoch MAP <70 mmHg (in-room to surgical end) | 22  | 10-35| 49.5   | 36-57| 14     | 13-18| 0.364 |
| #epoch HR <50 bpm (in-room to surgical start) | 0   | 0-0  | 0      | 0-1  | 0      | 0-0  | 0.584 |
| #epoch HR <60 bpm (in-room to surgical start) | 0   | 0-2  | 2      | 0-4  | 0      | 0-1  | 0.639 |
| #epoch HR >100 bpm (in-room to surgical start) | 1   | 0-2  | 0      | 0-0  | 0      | 0-1  | 0.086 |
| #epoch HR >120 bpm (in-room to surgical start) | 0   | 0-0  | 0      | 0-0  | 0      | 0-0  | 0.220 |
| #epoch HR <50 bpm (surgical start to end) | 2   | 0-6  | 0      | 0-1  | 0      | 0-0  | 0.239 |
| #epoch HR <60 bpm (surgical start to end) | 4   | 0-14 | 3.5    | 0-7  | 0      | 0-0  | 0.564 |
| #epoch HR >100 bpm (surgical start to end) | 6   | 1-13 | 0      | 0-0  | 1      | 0-5  | 0.269 |
| #epoch HR >120 bpm (surgical start to end) | 0   | 0-9  | 0      | 0-0  | 0      | 0-2  | 0.158 |
| #epoch HR <50 bpm (in-room to surgical end) | 2   | 0-9  | 0      | 0-2  | 0      | 0-0  | 0.249 |
| #epoch HR <60 bpm (in-room to surgical end) | 4   | 0-14 | 4      | 0-8  | 0      | 0-0  | 0.580 |
| #epoch HR >100 bpm (in-room to surgical end) | 8   | 1-13 | 0.5    | 0-1  | 2      | 1-5  | 0.279 |
| #epoch HR >120 bpm (in-room to surgical end) | 0   | 0-9  | 0      | 0-1  | 0      | 0-2  | 0.194 |

# Number of, each epoch was 10 min. IQR: Intraquartile range. BMI: Body mass index. ASA: American Society of Anesthesiologists. HR: Heart rate, MAP: Mean atrial pressure, OPCAB: Off-pump coronary artery bypass surgery.
procedure and the number of epochs of heart rate <50 and 60 beats/min were associated with greater base deficits [Table 2].

Adjusting for other factors, we initially found that the Mini-Maze procedure was associated with a greater base deficit than off-pump CABG, exhibiting a 2.63 mEq/L (95% CI: −5.39–0.13) greater base deficit [Table 3]. However, after forcing surgery type, diabetes, and their interaction into the model, none of the factors was statistically significant [Table 4]. In our final multivariate model, using Akaike information criteria to adjust for all other factors, diabetes mellitus (estimate = −2.87, 95% confidence interval = −5.55–−0.19), but not surgery type, was associated with base deficit [Table 5].

DISCUSSION

In our original hypothesis, we proposed that the Mini-Maze procedure is associated with and may directly contribute to the development of a clinically significant metabolic acidosis. However, after adjustment for other factors, including diabetes, we found that the absence of diabetes, but not the Mini-Maze procedure, was associated with the greater base deficit [Tables 3-5].

In the hierarchical regression, our initial finding that Mini-Maze was associated with the greater base deficit was replaced by diabetes. This analysis can be attributed to the fact that no patients in the Mini-Maze group have diabetes mellitus, compared to 4 (33%) in the OPCAP group. Therefore, the Mini-Maze group was not associated with a postoperative base deficit; rather, the type of surgery was acting as a partial surrogate for being nondiabetic. In our final model, if the patient had diabetes, they experienced a smaller base deficit, and if they are nondiabetic, they experience a larger base deficit.

Why would diabetes be associated with less base deficit? Given that patients with insulin control of diabetes mellitus suffer from either insulin resistance, a lack of endogenous insulin production, or a combination of the two and are prone to hyperglycemia, one would expect some diabetic patients to develop lactic acidosis from the metabolism of ketone bodies. Yet, our observations and our model found the opposite circumstance: A patient with diabetes experiences less base deficit than a nondiabetic patient. While acidosis can be prevented by even small amounts of insulin, it should not produce an alkalosis. Rather, the explanation may be found in the less frequently discussed physiologic effects of insulin that are independent of glucose homeostasis.

A landmark and now controversial clinical investigation in 2001 demonstrated a decrease in morbidity and mortality in critically ill, predominantly cardiac surgical patients when intensive insulin therapy was used to achieve normoglycemia. While the recommended degree of glucose control varies from one study to the next, it is unlikely that the benefit of insulin therapy stems solely from its influence on the glucose concentration in the bloodstream. In addition to insulin’s ability to increase glucose uptake into cells and promote adenosine triphosphate production via

Table 2: Univariate linear regression of factors associated with amount of postoperative base deficit

| Factor                                      | Estimate | 95% CI      | P     |
|---------------------------------------------|----------|-------------|-------|
| Mini-Maze compared to Conventional Maze group | 2.90     | 0.19-5.61   | 0.041 |
| Male sex                                    | −1.88    | −4.27-0.51  | 0.132 |
| Weight (kg)                                 | −0.03    | −0.08-0.02  | 0.197 |
| BMI (kg/m²)                                 | −0.12    | −0.28-0.05  | 0.178 |
| Diabetes on Insulin                         | −3.83    | −6.94–−0.71 | 0.022 |
| #epoch HR <50 bpm (surgical start to end)   | 0.28     | −0.02-0.57  | 0.074 |
| #epoch HR <60 bpm (surgical start to end)   | 0.11     | 0.00-0.23   | 0.064 |
| #epoch HR <60 bpm (in-room to surgical end) | 0.27     | −0.01-0.55  | 0.065 |
| Preoperative anion gap (mEq/L)              | 0.11     | 0.00-0.22   | 0.064 |

*: Number of, each epoch was 10 min. BMI: Body mass index, HR: Heart rate, CI: Confidence interval

Table 3: Model of factors independently associated with base deficit (including group)

| Factor                                      | Estimate | 95% CI      | P     |
|---------------------------------------------|----------|-------------|-------|
| Intercept                                  | 22.93    | 8.86-37.00  | 0.004 |
| Off-pump CABG group                        | −2.63    | −5.39-0.13  | 0.073 |
| Conventional Maze group                    | −2.06    | −5.44-1.32  | 0.243 |
| Weight (kg)                                | −0.07    | −0.11-0.02  | 0.010 |
| Preoperative serum creatinine (mg/dL)      | 1.93     | 0.49-3.38   | 0.014 |
| Preoperative bicarbonate (mEq/L)           | −0.34    | −0.74-0.06  | 0.105 |
| Preoperative anion gap (mEq/L)             | −0.43    | −0.93-0.07  | 0.101 |
| Fluids out (mL)                            | −0.001   | −0.003-0.0003 | 0.116 |

CI: Confidence interval, CABG: Coronary artery bypass grafting
glycolysis, insulin also causes arterial vasodilation and capillary recruitment by activation of nitric oxide, improving myocardial perfusion.[11,12] Furthermore, the inotropic and direct cardioprotective effects of insulin have been found to be independent of blood glucose concentration.[13]

Given that insulin therapy has the ability to improve myocardial perfusion while promoting cardioprotection and inotropy, we suggest that these effects would help to mitigate the hypoperfusion and acidosis that routinely accompanies off-pump open heart surgery. While both diabetic and nondiabetic patients receive insulin to maintain normoglycemia during surgery, diabetic patients typically require higher concentrations of insulin to treat hyperglycemia, and would, therefore, benefit more from the perfusion-promoting effects of insulin. However, given the retrospective nature of this study, these assertions are speculative, and we suggest prospective studies to further investigate this topic.

We also found that creatinine, a marker of renal function, was associated with elevated base deficits, while greater fluid out, predominantly urine and to a lesser extent gastric, was associated with the smaller base deficit. The kidneys are essential for maintaining homeostasis of blood volume, waste products, electrolytes, as well as acid-base equilibrium. Renal dysfunction impairs the body’s ability to maintain this homeostasis, particularly the kidney’s ability to reabsorb bicarbonate and buffer perturbations in plasma acid content. Increased urine output can lead to a contraction alkalosis while gastric drainage with its loss of HCl leads to a metabolic alkalosis, which would contribute to the smaller base deficits we found with increased fluid out.

One of the strengths of this study is the use of the electronic health record to evaluate intraoperative hemodynamics. An advantage of obtaining data from real-time EMR information capture is the temporal fidelity and recording accuracy with which the information is recorded, allowing for a more accurate examination of hemodynamics than would be possible for hand-written records. While there were univariate associations between heart rate and base deficit, these did not persist after adjustment by the other factors. Another very important strength of this study’s design is the inclusion of two control groups, the conventional MAZE group, and the OBCAB group. This provided a contextual framework as the conventional Maze procedure is similar to the Mini-Maze in the type and extent of direct cardiac injury from the ablation while the OPCAB group is similar to the Mini-Maze procedure in mechanically restricting and stabilizing the heart, while avoiding cardiopulmonary bypass. A final strength of our study is the use of Akaike information criterion to construct our models. Akaike information criterion uses information theory to assess the tradeoff between the goodness of fit and complexity of the model.

There are several limitations to our study. First, as we only measured base deficit in this study and not the type of acid accumulating, we are limited in not being able to discriminate between lacto- and keto-acidosis. Further study is indicated to determine the types and amounts of acids produced. Second, there was a sex imbalance between the groups, with the Mini-Maze group including the least women. However, we adjusted...
for this in our multivariable analyses. Third, with only 36 subjects in three groups we are at increased risk of both Type I error, in accepting diabetes as associated with the base deficit, and Type II error, in rejecting Mini-Maze as associated with the base deficit. However, the Mini-Maze is still a relatively novel and uncommon operation. As the operation becomes more common, future studies with larger populations will be possible. Finally, the study was conducted in only one center and may not generalize to centers that perform these operations with different techniques or different anesthetics.

CONCLUSION

We found that the Mini‑Maze procedure was not associated with a larger base deficit. Instead, nondiabetic patients and patients with higher creatinine were associated with greater base deficits after undergoing cardiac surgery.

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Conflicts of interest
There are no conflicts of interest.

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