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# Journal of Composites and Compounds

## The role of ionised magnesium compound in cardiac surgery

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### ABSTRACT

**Patients:** This was a clinical study of ionized and total magnesium compounds in 30 patients, assessed perioperatively, when undergoing Coronary Artery Bypass Graft (CABG) procedures. The mean age of the patients (3 females and 27 males) was 61.6±9.6 years, ranging from 35-76 years. All patients underwent a CABG with an average duration of cardiopulmonary bypass of 79.2 ±26.9 minutes. Patients with a history of renal insufficiency, pulmonary disease, implanted pacemaker or any previous cardiac operation were excluded from the study.

**Investigations:** Total and ionized magnesium, and calcium compounds in serum, as well as Na<sup>+</sup>, K<sup>+</sup>, phosphate, creatinine, urea, cholesterol, triglyceride, protein, and albumin were assessed perioperatively. These were characterised as before induction of anesthesia (Point A), after cardiopulmonary bypass (Point B), one hour after admission to intensive care unit (Point C), and the next postoperative morning (Point D).

**Result:** Only one (3%) patient showed preoperative ionized hypomagnesemia, and another one (3%) showed hypermagnesemia. Following the CABG procedure, (Point B), ionized magnesium levels were statistically reduced ( $p<0.0001$ ) followed by a gradual elevation which reached almost initial values (Point A versus Point D,  $p>0.05$ ). There did not seem to be any influence of one form of magnesium compound on another. The total postoperative rhythm disturbances (14/36), which needed therapy in the intensive care unit, showed 8 out of 30 (26%) of patients had ionized hypomagnesemia. No correlation was detected between spontaneous cardiac action after termination of the cardiopulmonary bypass, duration of ventilatory support and ionized magnesium levels. Nevertheless, there was a correlation between catecholamines levels and hypomagnesemia ( $p<0.05$ ).

**Conclusion:** The conclusion of this study was that determination of ionized magnesium compounds is important in predicting the pathological state of patients undergoing CABG. This helps to minimise perioperative morbidity.

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Peer review under responsibility of UGPH.

### ARTICLE INFORMATION

#### Article History:

Received 11 December 2024

Received in revised form 23 January 2025

Accepted 19 February 2025

#### Keywords:

Hypomagnesemia  
Ionised magnesium compound  
Perioperative morbidity

## 1. Introduction

Magnesium plays a critical role in many cardiovascular processes, including nitric oxide synthesis, coronary reactivity, vascular smooth muscle tone, transmembrane calcium flux, potassium transport and myocardial conduction and contractility [1, 2]. The total magnesium content of each human being is approximately 20 mmol/kg of fat-free tissue or an approximate total of 24g [3, 4]. Serum magnesium exists in three fractions: free ionized magnesium [5] (approximately 70-80%), complex bound

magnesium [6] (approximately 1-2%) and protein-bound fraction [7] (approximately 20-30%). The free, or ionized form of magnesium (Mg<sup>2+</sup>) is physiologically active and therefore is clinically the most important analyte [8]. Ionised magnesium compound is the second most abundant intracellular cation (next to ionised potassium) and the fourth most abundant cation in the body [9]. Mg<sup>2+</sup> is a cofactor which catalyses or activates more than 325 enzymes in the body[10]. It is pivotal in the transfer, storage and utilization of energy [11]. A number of reports have shown that magnesium is important in myocardial injury [12],

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<https://doi.org/10.61186/jcc.7.1.2> This is an open access article under the CC BY license (<https://creativecommons.org/licenses/by/4.0/>)

dysrhythmia [13], hypercoagulation [14], atrial hypertension [15] and coronary vasospasm [16].

It is important to note that the level of total magnesium (TMg) is not directly proportional to  $Mg^{2+}$ , therefore  $Mg^{2+}$  cannot be predicted from TMg [17]. It is therefore essential to directly measure the ionized fraction of magnesium in clinical analysis. Cardiac surgery, particularly coronary artery bypass grafting (CABG), is associated with significant physiological and biochemical changes [18]. In this context, magnesium, especially its ionized form ( $Mg^{2+}$ ) compound, plays a critical role [19]. Ionized magnesium, as a major intracellular cation, is essential for regulating cardiac processes such as electrical conduction, myocardial contraction, and energy transfer [20].

Studies have shown that low  $Mg^{2+}$  levels can increase the risk of arrhythmias, myocardial injury, and other complications. Moreover, since total magnesium (TMg) levels do not directly reflect ionized magnesium, it is crucial to measure  $Mg^{2+}$  directly for accurate clinical assessment and optimal patient management [21, 22].

Other researcher has studied magnesium in relation to CABG procedures emphasising the need for accurate and reproducible laboratory analysis to optimise patient outcome [21, 23]. The goals of this clinical study were to assess the perioperative change in the level TMg and  $Mg^{2+}$  measured by using ion selective electrodes (ISE). The impact of the range of magnesium levels, on the perioperative course of patients following CABG, will be discussed.

## 2. Materials and methods

### 2.1. Patients

Thirty patients with an age ranging from 35 to 76 years (mean age  $61.5 \pm 9.6$  years) at the time of surgery underwent isolated CABG at the Zurich University Hospital. There were 27 males and 3 females in the patient group. Patients with a history of renal insufficiency, pulmonary disease, an implanted pacemaker or any previous cardiac surgery were excluded from the study. All patients in the study had neither chronic obstructive pulmonary disease, implanted pacemakers nor any previous heart surgery in their anamnesis.

Patients with metabolic disorders such as diabetes mellitus or renal failure were excluded. Table 1 shows the demographics and clinical data of the patients. Fourteen patients had myocardial infarction (MI) in their anamnesis, among this one patient developed a recurrent infarction. Twenty-two patients were taking antiarrhythmic medication before surgery. All patients underwent a CABG procedure according to standard technique and magnesium was not used in cardioplegia. Priming contained 2.5 mval magnesium.

**Table 1**  
Demographics and Clinical Parameters of CABG patients.

|  |                                     |
|--|-------------------------------------|
| Total patients (n):                        | 30                                  |
| males                                      | 27                                  |
| females                                    | 3                                   |
| Mean age (years)<br>(range)                | $61.6 \pm 9.6$<br>(35-76)           |
| History of MI                              | 14<br>(1 patient with reinfarction) |
| Arterial hypertension                      | 15                                  |
| Preoperative medication: $\beta$ -blockers | 15                                  |
| Ca-antagonist                              | 4                                   |
| Digoxin                                    | 3                                   |
| Left ventricular EF* (%)                   | $51.3 \pm 16.7$                     |
| Duration of bypass (minutes)               | $79.2 \pm 26.9$                     |
| Aortic cross-clamp time (minutes)          | $48.7 \pm 19.8$                     |
| Number of distal anastomoses               | $4.0 \pm 1.2$                       |

\*EF- Ejection Fraction.

### 2.2. Analysis

The following analytes were tested perioperatively: TMg,  $Mg^{2+}$ , total Ca (TCa), free ionized calcium ( $Ca^{2+}$ ), potassium ( $K^+$ ), sodium ( $Na^+$ ), phosphate, creatinine, urea, cholesterol, triglyceride, total protein compounds, albumin and pH in order to observe their impact on the perioperative magnesium range. Blood specimens (5mL) were drawn from the intravenous line, using standard red-top vacutainer tubes containing 14.3 units of heparin per mL of sample. This sampling procedure took place at four times:

- Point A: Before induction of anesthesia.
- Point B: After termination of CPB (Cardiopulmonary Bypass).
- Point C: One hour after admission to ICU (Intensive Care Unit).
- Point D: The first postoperative morning.

The samples were immediately sent for analysis to the laboratory, where they were kept at room temperature for less than 1 hour and centrifuged for 10 minutes to obtain clear plasma. The plasma was transferred immediately into a microtube (1.5 ml polypropylene, Sarstedt Germany) and capped. The pH-corrected  $Ca^{2+}$  and  $Mg^{2+}$  concentrations were determined using an Ion-Selective Electrode (ISE) of the NOVA 8 Electrolyte Analyzer (NOVA Biomedical). This instrument is designed for simultaneous measurements of  $Na^+$ ,  $K^+$ , hematocrit, pH, actual or pH-corrected  $Mg^{2+}$  and  $Ca^{2+}$  in whole blood, plasma and serum.

The hemodynamic postoperative course of the patients (particularly rhythm disturbances) was documented through continuous monitoring in the ICU and periodical ECG assessment in the general ward.

### 2.3. Statistical analysis

All results are expressed as mean $\pm$ SD values. A Student's t-test was used where appropriate. Correlation analysis between various parameters was performed with Pearson method. For all comparisons,  $p<0.05$  was taken as statistically significant.

## 3. Results and discussion

The characteristics of the patients, the history of disease and the surgical result is listed in Table 1. In 4/26 (15%) of cases heart activity after termination of distal anastomoses was stimulated by means of a single artificial defibrillation. Defibrillation was needed twice in 25% of patients. In 10 (38%) of cases it was necessary to prescribe catecholamines to treat complications. In all of these patients, both fractions of magnesium were lowered. The values of perioperative measured analytes are shown in Table 2. Perioperatively, only 1 (3%) patient had ionized hypomagnesemia and another 1 (3%) had ionized hypermagnesemia in the Point A sample. Postoperatively (Point B samples) the  $Mg^{2+}$  compounds values were significantly lower ( $p<0.0001$ ). The next samples (Point C) had a tendency to increase slightly and in Point D samples reached almost the initial data (A versus D,  $p>0.05$ ). In 10 patients (33%), 22 mval of magnesium was administrated during the CABG procedure. In all of these cases an increase in  $Mg^{2+}$  and TMg was observed at  $0.18 \pm 0.05$  (33 $\pm$ 9%) and  $0.29 \pm 0.08$  (38 $\pm$ 11%) respectively. There was a total of 36 cases of dysrhythmia during the stay in ICU. Among these patients 14 cases needed treatment. In the general ward it was necessary to treat 6 out of 7 dysrhythmia cases. Different kinds of dysrhythmias were seen and some patients showed more than one dysrhythmia. These are shown in Table 3. The postoperative stays in the ICU mainly lasted not more than 24 hours except for 3 (10%) patients.

**Table 2**  
Analyte data.

| Elements                    | Normal range    | Point A                | Point B               | Point C               | Point D               |
|-----------------------------|-----------------|------------------------|-----------------------|-----------------------|-----------------------|
| Mg <sup>2+</sup>            | 0.4-0.60 mmol/l | *0.50±0.06 (0.34-0.59) | 0.44±0.07 (0.32-0.54) | 0.45±0.06 (0.37-0.57) | 0.47±0.07 (0.32-0.63) |
| TMg                         | 0.65-1.0 mmol/l | 0.74±0.07 (0.59-0.83)  | 0.65±0.05 (0.54-0.76) | 0.67±0.08 (0.55-0.98) | 0.77±0.21 (0.56-1.58) |
| Mg <sup>2+</sup> /TMg ratio | %               | 0.67±0.08 (0.47-0.82)  | 0.68±0.09 (0.48-0.91) | 0.68±0.08 (0.56-0.84) | 0.64±0.11 (0.33-0.81) |
| Ca <sup>2+</sup>            | 1.1-1.30 mmol/L | 1.18±0.09 (0.89-1.31)  | 1.07±0.11 (0.74-1.21) | 1.09±0.08 (0.84-1.23) | 1.10±0.10 (0.72-1.20) |
| TCa                         | 2.1-2.6 mmol/L  | 2.08±0.13 (1.80-2.30)  | 1.77±0.19 (1.18-2.17) | 1.81±0.13 (1.62-2.13) | 1.99±0.10 (1.79-2.25) |
| Ca <sup>2+</sup> /TCa ratio | %               | 0.57±0.04 (0.48-0.66)  | 0.61±0.10 (0.42-1.00) | 0.60±0.05 (0.49-0.69) | 0.55±0.06 (0.36-0.65) |
| Na <sup>+</sup>             | 135-145 mmol/L  | 139.6±2.2 (136-144)    | 137.0±2.3 (132-142)   | 138.3±2.0 (134-142)   | 137.7±2.2 (134-144)   |
| K <sup>+</sup>              | 3.5-4.5 mmol/L  | 3.6±0.3 (2.9-4.0)      | 4.0±0.5 (3.3-5.2)     | 4.0±0.3 (3.5-4.6)     | 4.2±0.3 (3.7-4.7)     |
| Phosphate                   | 0.6-1.3 mmol/L  | 1.01±0.13 (0.77-1.33)  | 0.78±0.17 (0.49-1.09) | 0.80±0.18 (0.49-1.11) | 0.87±0.21 (0.56-1.32) |
| Creatinine                  | 70-105 umol/L   | 84.7±13.6 (59-111)     | 77.0±12.4 (53-99)     | 79.4±13.1 (54-100)    | 90.0±18.4 (60-130)    |
| Urea                        | 2.5-8.0 mmol/L  | 4.9±1.4 (2.5-7.7)      | 4.7±1.4 (2.4-7.3)     | 4.6±1.2 (2.7-6.7)     | 4.5±1.1 (2.4-7.0)     |
| Cholesterin                 | 0.5-2 mmol/L    | 4.3±1.1 (2.1-6.0)      | 2.9±0.5 (1.7-3.9)     | 2.8±0.5 (1.7-3.9)     | 2.0±0.5 (1.2-3.1)     |
| Triglyceride                | 0.5-1.6 mmol/L  | 1.78±1.37 (0.63-5.77)  | 0.87±0.53 (0.28-2.27) | 1.12±0.68 (0.33-2.98) | 1.04±0.59 (0.27-2.50) |
| Protein                     | 65-80 g/L       | 56.7±7.4 (41.0-69.0)   | 40.2±6.1 (33.0-57.0)  | 43.7±7.6 (35.0-63.0)  | 53.2±5.7 (44.0-64.0)  |
| Albumin                     | 40-50 g/L       | 33.7±4.9 (23.0-41.0)   | 25.1±4.8 (19.0-41.0)  | 29.2±6.8 (20.0-47.0)  | 38.7±5.0 (28.0-48.0)  |

**Note:** In the table the values of the patients after intravenous magnesium administration are excluded. \*Upper data are mean values with standard deviation; lower data are range of values. Point A - Preoperative; Point B - Post-bypass; Point C - ICU One hour after the operation; Point D - First postoperative day TMg - Total Magnesium; Mg<sup>2+</sup> - Ionised Magnesium; TCa - Total Calcium; Ca<sup>2+</sup> - Ionised Calcium.

**Table 3**  
Postoperative cardiac rhythm disturbance following CABG.

| Arrhythmias                   | ICU* | Therapy needed | General ward | Therapy needed |
|-------------------------------|------|----------------|--------------|----------------|
| Bradycardia                   | 2    | 2              | 0            | -              |
| Supraventricular tachycardia  | 1    | 0              | 0            | -              |
| Supraventricular extrasystole | 10   | 0              | 0            | -              |
| Ventricular extrasystole      | 17   | 7              | 1            | 0              |
| Atrial fibrillation           | 3    | 2              | 5            | 5              |
| Ventricular tachycardia       | 3    | 3              | 1            | 1              |
| Total                         | 36   | 14             | 7            | 6              |

\*ICU- Intensive Care Unit.

These 3 patients had to remain in ICU for three days postoperatively because of reintubation due to rhythm disturbances and hemodynamic deterioration. 1 patient (3%) was transferred back to the ICU from the general ward due to an arrhythmia and was urgently intubated. The outcome was successful for all of patients. Patients, excluding the patient transferred back to ICU, were usually discharged from the hospital on the 7th postoperative day. Long-term antiarrhythmic therapy was prescribed for 5 (16%) patients because of postoperative atrial fibrillation. There was no hospital mortality. It is clear that magnesium plays a significant role in different physiological processes. A number of publications show abnormal magnesium levels implicated with hospital morbidity and mortality [24]. Magnesium levels are important in the management and outcome of cardiac patients [25]. ISE technology was used to assess Mg<sup>2+</sup> compounds and to assess the potential influence of magnesium on the perioperative course of CABG patients. The normal range for Mg<sup>2+</sup> in this study is lower than that mentioned in early work [26]. Contrary to other researches [27, 28] in this investigation it was noted that most of the preoperative patients were normal for both Mg<sup>2+</sup> and TMg. Only 1 (3%) patient had hypomagnesemia, while in 4 (13%) of the patients TMg was decreased. These results differ from those of other authors who reported 32-34% of patients with TMg hypomagnesemia [29, 30]. Another study by B. T. Altura et al.[31] has reported a much higher percentage of Mg<sup>2+</sup> (57-71%). These differences may be explained by the fact that the patients in this study were not critically ill and their base magnesium level was therefore not needed for physiological homeostasis [32]. The patients were electively hospitalized the day before surgery. Nevertheless, Mg<sup>2+</sup> was high in one patient (3%) in this study even though his TMg was normal. This may reflect the unreliability of TMg testing reported in the literature where up to 80% of low TMg results may be considered to be erroneous [33]. In this study both forms of magnesium compounds (TMg and Mg<sup>2+</sup>) were reduced following termination of CPB. This may have been caused by

hemodilution during CPB [34]. In 7 cases (23%) intravenous magnesium (22 mval) was given intraoperatively. Therefore, in these patients Mg<sup>2+</sup> and TMg rose notably, 33±9 % and 38±11 % respectively, compared with initial values. It must, however, be mentioned that in 4 cases (13%) the values of Mg<sup>2+</sup> were above the normal range, while TMg remained within normal range. It is of interest that the pattern of magnesium levels seen in this study, including 7 (23%) patients with high values after magnesium administration, returned to their initial values over time. No equilibration was found between TMg and Mg<sup>2+</sup>. It is known that circulating protein levels (mostly albumin) alter the interpretation of magnesium status [35]. A decrease in albumin will lower TMg without affecting the Mg<sup>2+</sup> levels [36]. Phosphate, however, may bind to significant amounts of Mg<sup>2+</sup> *in vivo* [37]. In this study, there were no statistical differences found between Mg<sup>2+</sup> level alteration and other simultaneously measured analytes. During the postoperative stay in ICU there were 36 cardiac dysrhythmia events. Fourteen of these (39%) needed medical intervention. Seven patients (23%) had hypomagnesemia in ICU postoperatively (Point C samples). Three patients suffered serious arrhythmias (ventricular tachycardia, VT) in the ICU and their Mg<sup>2+</sup> was reduced. One patient in this group again developed VT on the fourth postoperative day in the general ward. Another patient with normal D-Mg<sup>2+</sup> levels also suffered VT in the general ward. These patients suffering VT in the general ward were transferred back to the ICU, reintubated and stayed under monitor-control until recovery. There were no hospital deaths among the patients in the study. It has previously been reported that patients who had hypomagnesemia on the first postoperative day had a significantly greater incidence of atrial fibrillation (AF) than those who were normomagnesemic (31% *versus* 10.3%) respectively [38]. We did not find this relationship in the current study. AF in our investigation, which needed medical intervention, occurred in 7 patients (23%). One patient developed AF in the ICU (3%) on

the day of surgery and the other 6 (20%) in the general ward. In the first case (AF in the ICU) it developed with a background of hypomagnesemia and it was suppressed with digoxin. In other cases of AF, in the general ward, actual magnesium levels at the time of developing AF were not known. In this study there was no correlation between spontaneous heart action after the main stage of surgical intervention and magnesium levels. In 4 (13%) cases was it necessary to resort to defibrillation. In the remaining 26 (87%) patients the heart began to contract spontaneously in spite of low magnesium, which was detected in the Point B samples.

The present study agrees with the concept that catecholamines cause hypomagnesemia as a result of intracellular magnesium shift [39, 40]. This study found a significant correlation ( $p<0.05$ ) between catecholamine levels and deterioration of magnesium levels. Some researchers have previously reported respiratory muscle weakness attributed to magnesium deficiency [26, 41]. The present study does not agree with this observation as 26 (87%) of our patients could be extubated within the first 24 hours after surgery and this was independent of the magnesium level.

A variety of anions (acetate, bicarbonate, heparin, citrate, lactate, phosphate and sulphate) may bind to  $Mg^{2+}$  and hence appreciably reduce extracellular  $Mg^{2+}$  (4-90%) [42].

At the same time, TMg should remain unchanged, or actually increase if intracellular  $Mg^{2+}$  diffused out of the cells to re-establish an equilibrium between intracellular and extracellular  $Mg^{2+}$  [43]. This suggests that the  $Mg^{2+}$  / TMg ratio should vary over time. In this study  $Mg^{2+}$  / TMg ratios in the first three samples (Point A to Point C) were constant (average 67%, 68%, 68%) but in the Point D samples there was a significant depression (64%). From these data we assume that  $Mg^{2+}$  reduces to approximately 64% on average and subsequently more  $Mg^{2+}$  (36%) is bound to protein or various ligands.

## 4. Conclusion

This study has shown that magnesium is significantly reduced during and after cardiac surgery (CABG) and that directly measured  $Mg^{2+}$  recovers to 90% by 24 hours after surgery. Nevertheless, the  $Mg^{2+}$  / TMg compounds ratio, which reflects the percentage of  $Mg^{2+}$  available, reduced post-operation in this study. Taking into consideration that catecholamines, extracorporeal circulation, protamine and albumin levels may influence magnesium levels, it is important to determine perioperative magnesium levels in patients undergoing CABG. Since a reduction in magnesium is correlated with various dysrhythmias, it is essential to provide magnesium supplementation where indicated. The amount of magnesium to be administrated, and in which period of the patient's hospital course, depends on the judgement of the physicians caring for the patients. The medical literature contains conflicting opinions concerning this question [44-46].

## Author contributions

**Tengiz Tkebuchava:** Conception and design of the study, acquisition of data, or analysis and interpretation of data, drafting the article or making critical revisions related to relevant intellectual content of the manuscript and final approval of the version of the article to be published. **Anna Tkebuchava:** Analysis and interpretation of data, drafting the article or making critical revisions related to relevant intellectual content of the manuscript. **Peter Hollands:** Analysis and interpretation of data, drafting the article or making critical revisions related to relevant

intellectual content of the manuscript and final approval of the version of the article to be published.

## Funding

No funding was received for this study.

## Conflict of interest

The authors declare no conflict of interest.

## Data availability

All data generated or analyzed during this study are included in this published paper.

## Ethical issues

This case report was conducted in accord with the World Medical Association Declaration of Helsinki. Patient's parents have given us a written informed consent for publication. Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors.

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