**Review**

**Monitoring magnesium to guide magnesium therapy for heart surgery**

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**Introduction**

For many years it has been recognized that magnesium levels play an important role in morbidity associated with heart surgery. However, considerable confusion exists in the literature concerning whether Mg should be administered to these patients, and, if so, how much and when. The goals of this paper are to review (1) methods used to evaluate Mg status in patients, (2) causes and consequences of abnormal Mg levels perioperatively, (3) outcome improvements and risks with Mg supplementation, and (4) guidelines for administering Mg therapy.

**Methods used to evaluate Mg status in patients**

**Physiological indicators**

Pulse, mean arterial pressure, deep tendon reflexes, hourly diuresis, respiratory recordings, and hypotension are used to monitor Mg status in patients [1]. Significant prolongation of intraatrial and atrioventricular (AV) nodal conduction times, as seen by ECG, may also reflect Mg activity [2].

**Mg measurement**

**Total magnesium (TMg)** represents the concentration of Mg present in blood plasma or serum. TMg, a measure of all of the Mg in the plasma or serum sample, equals protein-bound Mg plus ligand-bound Mg plus ionized Mg (iMg). Measurement of TMg requires the isolation of plasma (centrifugation of blood sample) or serum (clotting and centrifugation of blood sample). Measurement is made by atomic absorption spectrophotometry or colorimetry. Reference values for plasma and serum TMg typically range from 0.66 to 1.07 mmol·l⁻¹. There is virtually no correlation between plasma/serum TMg and intracellular TMg.

**Ionized magnesium (iMg = Mg²⁺)** represents the activity of unbound Mg in whole blood plasma, plasma, and/or serum. It is the physiologically active Mg fraction, i.e., the fraction to which tissues respond. Reference values typically range from 0.45 to 0.62 mmol·l⁻¹. The fact that it can be measured in a whole blood sample by electrode produces a rapid result (<150 s) on a small sample (≤200 µl). A rapid result can be very helpful for patients (1) with arrhythmia, (2) with changes in cardiac output, (3) receiving cardiovascular drugs, (4) sustaining hypoxic damage, and (5) receiving Mg therapy. Blood plasma iMg correlates with intracellular iMg and therefore represents a better indicator of Mg status than TMg. It is typically 70% of the TMg value, but varies with the protein and small ligand concentrations in the blood. The iMg value may be substantially less than 70% of the TMg value in critically ill patients where binding ligand concentrations (heparin, citrate, lactate, phosphate, bicarbonate, etc.) have increased.

Comparisons of iMg to TMg were illustrated in nine clinical settings (hypertension, acute myocardial infarction, head trauma, noninsulin-dependent diabetes, stroke, pregnancy, ischemic heart disease, cyclosporin recipients, and asthma) [3]. Ionized magnesium was found to be a better indicator of disease than TMg. In summary, iMg (1) represents the physiologically important Mg measurement, (2) is a better indicator of disease than TMg, and (3) is a more rapid measurement.

The literature should be interpreted with caution. Frequently, if not generally, the Mg values reported in
the literature are TMg, even though they may be reported as Mg\(^{2+}\). Measurement of iMg has recently been made possible (early 1990s), but this does not change the fact that many recent papers reporting Mg\(^{2+}\) really mean TMg.

Causes and consequences of abnormal Mg levels perioperatively

Presurgery

Although TMg deficiency is rare in healthy subjects, 16% of 98 heart surgery patients were hypomagnesemic [4]. Kidney disease, reduced glomerular filtration rate (<30 ml·min\(^{-1}\)) [2], reduced tubular reabsorption (frequently caused by the use of diuretics), reduced oral intake, and intravenous fluids with inadequate Mg led to abnormal Mg levels in these patients. Patients receiving digoxin for heart failure had preoperative total hypomagnesemia more frequently than patients not on digoxin (36% vs 10%) [4]. A history of high-grade ventricular dysrhythmia was associated with significantly lower preoperative mean TMg [4]. Patients who may have asymptomatic hypomagnesemia presurgery may then undergo a surgical procedure that, in the perioperative period, can cause them to progress to symptomatic hypomagnesemia [5]. Hyperaldosteronism [6] and noradrenaline [7] also promote hypomagnesemia.

During surgery

The frequency of hypomagnesemia increased to 71% (71/100 patients) following cardiopulmonary bypass (CPB) surgery [8]. Several factors reduce Mg concentration during surgery. These include hemodilution from prime volume [9], chelation of iMg by heparin and acid-citrate-dextrose when donated blood is used to prime the CPB circuit [9], and intramyocyte hypoxia [10–12]. In recently introduced off-pump coronary artery bypass grafting (CABG) surgery, many patients are not receiving Mg supplementation, and, consequently, are hypomagnesemic postsurgery (TMg averaging 0.61 mM after surgery) [13]. Magnesium administration (via cardioplegia, bolus doses, and fluid supplements) can minimize Mg depletion, if not lead to hypermagnesemia, perioperatively.

Outcome improvements and risks with magnesium supplementation

Adequate Mg levels are required for normal cardiovascular activity (conduction and contraction), tissue protection from oxygen free radicals and the inflammatory response, and blood flow. Table 1 identifies improvements in outcomes following cardiac surgery when Mg supplements were used.

Even though Mg supplementation provides strong benefits for the cardiac patient, the risks and complications of hypermagnesemia need to be considered. Hypermagnesemia may develop from inadequate renal function or high dosage levels of supplemented Mg. CPB surgery, itself, may cause renal failure sufficient to give hypermagnesemia with Mg therapy [35].

Hypermagnesemia can cause excessive flushing, sweating, warm sensations, hypotension, and vasodilation [5]. Magnesium may act as a laxative [1]. As an anticoagulant, Mg inhibits platelet aggregation, P-selectin expression, and fibrinogen binding to platelet GP IIb/IIIa receptor in vitro [36]. The number and energy of direct-current shocks to initialize and to sustain defibrillation was greatest in patients who received Mg therapy before bypass and in those whose plasma TMg was greater than 0.93 mmol·l\(^{-1}\) [37].

Table 2 presents a rough guideline correlating Mg values and clinical observations. Mg therapy in the immediate postoperative period following cardiac surgery can result in hypotension and bradycardia [5]. In one study, St. Thomas II cardioplegia solution, containing 16 mM MgCl\(_2\), was infused (10 ml·kg\(^{-1}\) every 30 min) during aortic cross-clamping [44]. Ionized magnesium levels of 1.5–1.58 mmol·l\(^{-1}\) were noted after unclamping. After discontinuation of extracorporeal circulation, vascular resistance decreased by 40%, while 78% (14/18) of patients required atrial or ventricular pacing in order to maintain a physiological level of heart rate for obtaining better hemodynamics. The hypotension and bradycardia extended the time for extracorporeal circulation.

### Table 1. Magnesium therapy improves clinical outcomes following heart surgery

- Arrhythmia reduced, with attendant reduction in morbidity and costs [5–7, 14–22]
- Fewer ischemic electrocardiograph changes [19]
- Decreased postoperative hypertension [19, 23]
- Decreased creatine kinase-MB isoenzyme levels [19, 24]
- Increased cardiac indices [4, 19, 25–27]
- Reduced postoperative pain and requirement for analgesics [19]
- Increased coronary flow [25]
- Decreased coronary vasospasms [28–30]
- Prolonged neuromuscular blockade [31]
- Reduced inflammatory response [32]
- Reduced platelet function [33]
- Reduced mortality [23, 34]
- Protects ischemic myocardium from Ca overload [33]
- Reduced cell necrosis from free radicals [33]
- Reduced ventilation requirement [4, 8]

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Table 2. Rough guideline correlating Mg values and clinical observations

- 0.6–1.0 mmol·l\(^{-1}\): Normal range
- 1.0–1.5 mmol·l\(^{-1}\): Mild hypermagnesemia
- 1.5–1.8 mmol·l\(^{-1}\): Moderate hypermagnesemia
- >1.8 mmol·l\(^{-1}\): Severe hypermagnesemia

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