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Review on the diagnostic role of cardiac troponins in pediatrics

Cardiac troponins (cTn) are biochemical markers of myocardial injury with unquestionable significance in diagnostic strategy in adults. In this paper we make an attempt to review the possible use of cardiac troponins in pediatric patients. However, they have not been used routinely in neonates and children, so far.

Cardiac troponins are protein components of the troponin-tropomyosin complex in myocardium. The complex consists of troponin C, troponin I (cTnI), troponin T (cTnT) and tropomyosin. Since troponins do not occur in extracellular space, their appearance in serum is a sensitive and specific marker of myocardium damage (15). Unlike troponin C, myoglobin, creatine kinase myocardial band and isoenzyme (CK-MB), both cardiac troponins: cTnT and cTnI are present only in myocardium and not in other tissues (10, 15). Troponins appear in blood in 2 to 4 hours after insult, peak in about 12 h, and then remain elevated for 7–10 days (3, 15).

Sensitivity of both cTnT and cTnI in the diagnosis of myocardial damage is clinically almost equal. They differ in intracellular compartmentation, biological half-life and molecular weight (1). There are also differences in the standardization and availability of commercial troponin kits. cTnT serum concentrations are evaluated by the use of two methods with comparable results. There are numerous methods used to evaluate cTnI, from different producers, differing with antibodies, their labelling, measurement techniques and calibration methods. Absolute values of gained results are often incomparable, however, diagnostic features of particular methods are similar.

Basic clinical application of serum cTn evaluation in adults are (15): • diagnosis of myocardial infarction (also perioperative infarction in patients undergoing cardiocurgery procedures) • reperfusion treatment efficacy evaluation in acute myocardial infarction • risk stratification in acute coronary disease • cardiomyocytes injury detection in other diseases (pulmonary embolism with right ventricle overload, pericarditis, myocarditis, sepsis and shock, use of cardiotoxic drugs, heart injury, chronic renal insufficiency, hypothyreosis).

In the literature, the following applications of cTn in pediatrics are mentioned:

Acute myocarditis is a disease that is difficult to diagnose by noninvasive methods within a short period of time. Endomyocardial biopsy with histopathology, immunohistology, and virus polymerase chain reaction have been studied with limited efficiency (17). In addition, these methods are less practical for pediatric patients because of the invasive nature. Considering the side-effects of treatment, a firm diagnosis is essential (17). Cardiac troponins have been found to be elevated in acute myocarditis in adult patients with higher sensitivity than from conventional methods (11). Therefore, a number of studies was performed to evaluate the diagnostic value of cTn in myocarditis in children. Masłowska et al. (14) determined the cTnT levels in children with different cardiac diseases. They revealed that cTnT was significantly elevated in children with acute

myocarditis, comparing to patients with congenital heart disease or cardiomyopathy. Soongswang et al. (16) in their paper tried to assess the use of serum cTnT level as a noninvasive indicator to differentiate acute myocarditis and chronic dilated cardiomyopathy in pediatric patients. They included 10 patients diagnosed to have myocarditis, 10 with chronic dilated cardiomyopathy and 21 controls with moderate left-to-right shunt. The study showed that cTnT levels were significantly higher for myocarditis than for dilated cardiomyopathy and left-to-right shunt with cardiac heart failure (CHF). The same author performed another study (17) to determine the cutoff point of cTnT level with acceptable sensitivity and specificity to diagnose acute myocarditis in children. This time cTnT levels were elevated in 24 patients diagnosed as acute myocarditis, 19 with idiopathic chronic dilated cardiomyopathy (DCM) and 21 patients with left-to-right shunt and chronic heart failure. Again the cTnT level was higher in patients with myocarditis than in the remaining groups. The level of 0.052 ng/ml was considered a suitable cutoff point to diagnose acute myocarditis. Summarizing, serum cTn levels seem to be valuable diagnostic marker of myocarditis in children, however there is still a need to confirm it in further studies performed on bigger groups of patients.

Asphyxia in newborns. In several studies cTn was measured in healthy and asphyxiated neonates. In studies in which the third-generation CTnT assay was used (2, 4, 13), a median value for healthy babies was reported effectively the lower limit of the assay or undetectable (0.01 ng/ml). Two of the cord blood studies reported the 75th percentile as 0.14 ng/ml (1, 10). Genser et al. (7) reported 150 neonates, of whom 35 were assumed to be asphyxiated as defined by umbilical arterial pH and Apgar scores together. CTnT levels were significantly higher in the 35 asphyxiated patients compared with 115 control subjects. Makikallio et al. measured cTnT in 66 neonates born after uncomplicated pregnancy and in 37 with severe placental insufficiency, which was accompanied by a rise in fetal systemic venous pressure. The neonatal cTnT were significantly increased in the presence of umbilical venous return, which indicated myocardial cell damage. A number of studies was also performed to evaluate cTn in preterm infants with respiratory distress syndrome (RDS) (5, 7, 18). The high cTnT concentrations in these patients suggest the presence of myocardial damage in neonates with RDS.

Perioperative myocardial injury in patients operated for congenital heart diseases. Immer et al. (9) measured cTnT levels in 60 patients before and after cardiac surgery. Except of four children all troponin values were within normal range in the preoperative period. All children with intracardiac surgery showed a postoperative increase in troponin T. Children with extracardiac surgery of great vessels showed no postoperative increase of troponin T. Some other preliminary data suggest that the magnitude elevation predicts the severity of illness in the immediate postoperative period as well as survival (10). Postoperative multicenter studies are needed to assess the predictive value of cTn elevation on survival after cardiovascular surgery in children (10).

Drug-induced cardiotoxicity. Cardiotoxicity is recognized as complication following mainly chemotherapy with anthracyclines or cyclophosphamide, but also after administration of terbutaline i.v. for severe asthma (1). Lipshultz et al. (12) evaluated cTnT levels in 15 children treated with doxorubicin for acute leukemia. Elevations of cTnT levels were noted in 7 children after their first dose of chemotherapeutic agent. Nine months later these children had echocardiographic evidence of thinner left ventricular walls. However, Fink et al. (6) in their study reporting 22 children treated with anthracycline did not find any significant elevations of cTn. It is clear that levels of cTnT should be measured in a larger cohort to identify the level that is followed by cardiomyopathy (10).

Cardiac transplantation. Significant advances have been made in management of the recipient after transplantation and attention is now directed to donor characteristics and outcome

after cardiac transplantation (10). Grant et al. (8) measured cTn levels in graft donors and related this levels to posttransplantation courses. They revealed that lower cTn levels were associated with better outcome in patients <1 year old. Elevated cTn levels indicate myocardial injury in graft before harvest. Further studies are needed to confirm that low cTn levels in graft donors are associated with better posttransplantation survival (10).

Serum measurements of cardiac troponins seem to be valuable also in some other disorders concerning children, such as Kawasaki disease or in children following resuscitation after cardiac arrest (1).

Cardiac troponins seem to have great diagnostic value not only in adults but also in pediatric patients with suspected myocardial damage. However, there is still need of new, big cohort studies before we could use them on routine to monitor treatment or to predict mortality and morbidity in sick children.

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SUMMARY

Cardiac troponins are of unquestionable role as markers of cardiac injury in adults. Attempts are now made to take advantage of diagnostic role of troponins in pediatric patients, however they are not used on routine yet. In our paper we present the possibilities of the use of these markers in sick children. Clinical situations such as acute myocarditis, asphyxia in newborns, respiratory distress syndrome, perioperative myocardial injury, drug-induced cardiotoxicity, cardiac transplantation and other are concerned.

Przegląd diagnostycznych zastosowań troponin sercowych w pediatrii

Troponiny sercowe mają ugruntowaną pozycję jako markery uszkodzenia mięśnia sercowego u dorosłych pacjentów. Podejmowane są próby diagnostycznego wykorzystania troponin w chorobach serca i innych u dzieci, jednak nie są one jeszcze stosowane rutynowo. W pracy przedstawiamy przegląd możliwych zastosowań tych markerów w pediatrii. Omówione są sytuacje kliniczne, takie jak: ostre zapalenie mięśnia sercowego, niedotlenienie okołoporodowe, zespół zaburzeń oddychania, okołoperacyjne uszkodzenie mięśnia sercowego, polekowe uszkodzenie serca, transplantacja serca i inne.