High-sensitivity cardiac troponins in health and disease

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Valorization

Introduction

The aim of this chapter is to address the possible opportunities for knowledge valorization based on the described research findings in this thesis. Knowledge valorization, knowledge transfer or commercialization are similar terms that all refer to the “process of creating value from knowledge, by making knowledge suitable and/or available for social and economic use and by making knowledge suitable for translation into competitive products, services, processes and new commercial activities”.[1,2]

Relevance

Acute myocardial infarction (AMI) and (unstable) angina, components of the clinical definition ‘(acute) coronary syndrome’, are major causes of death and disability worldwide.[3] In 2011, 9,876 individuals in the Netherlands died of coronary disease, with the majority of deaths (*n* = 6,467, 65%) resulting from AMI.[4] In the same year, 115,921 subjects with coronary disease were admitted to a hospital in the Netherlands, which accounted for 3% of all hospital admissions in the Netherlands in 2011.[4] This resulted in an economic healthcare burden of €2.1 billion, which corresponded to 2.3% of the total amount of healthcare costs in 2011 in the Netherlands.[5]

Patients with acute chest pain or other symptoms suggestive of AMI account for more than 10% of all emergency department consultations.[6] As the majority of these patients will be found not to have AMI, the diagnosis (rule-in) and rule-out of AMI seems to be equally important.[7] In addition, rapid and accurate diagnosis of AMI is of paramount clinical importance: delayed ‘rule-in’ of AMI increases morbidity and mortality, whereas delayed ‘rule-out’ causes anxiety in patients and excessive health care costs due to prolonged time spent at the emergency department.[8] Most patients with AMI have a non-diagnostic ECG and require serial blood sampling and measurement of cardiac troponins (cTn) as part of the clinical workup.[3] The clinical presentation of the patient, in conjunction with a typical ‘rise or fall’ of cTn concentrations between serial measurements, establishes the diagnosis.[3] In 2013, cTn were measured in 3,585 blood samples collected from patients presenting at the cardiac emergency department of Maastricht University Medical Center.

The analytical performance of the troponin assays has improved enormously over the last 5 years. Patients diagnosed with the ‘high-sensitivity’ (hs) troponin assays demonstrate a clear survival benefit compared to patients diagnosed with conventional troponin assays, due to an improved diagnostic sensitivity.[9] However, the diagnosis of AMI with the hs assays is more complex, which arises from the detection of previously unnoticed cTn elevations in patients with cardiomyocyte injury other than AMI.[10] This includes acute heart failure, type 2 diabetes, and even cTn elevations in healthy recreational athletes after an acute bout of endurance-type exercise. This lack in specificity is a challenge for clinicians. Therefore, it is essential to increase our understanding on how to interpret levels of cTn in settings of serial testing and endurance-type exercise.

On the contrary, the improvement in analytical sensitivity has resulted in more applications of cTn. Even when adjusted for traditional cardiovascular risk factors (such as smoking, diabetes, hyperlipidemia and hypertension), cTn concentrations below the clinical cut-off value for AMI measured in the general population are strongly associated with an increased risk of developing cardiovascular events and all-cause or cardiovascular mortality.[11] As traditional risk factors do not identify everyone who will eventually develop cardiovascular disease,[12] cTn are promising candidates to refine risk stratification models for the primary prevention of cardiovascular disease.

Target groups

Interpretation of troponin levels are mainly performed by clinicians (e.g. cardiologists, general practitioners) and laboratory specialists. In addition, the results described in this thesis could be of interest to diagnostic companies (e.g. Roche Diagnostics, Abbott Diagnostics, Beckman Coulter) that are involved with the development, optimization, implementation or application of a specific troponin assay. Research described in this thesis also has the potential to be of interest for (recreational) athletes.

Activities

The results described in this thesis can be translated into several activities or tools. These activities are clustered according to the three mechanisms of knowledge transfer; through results or commercialization, people and via cooperation *(figure 1)*.

This thesis describes the presence of a diurnal rhythm of cTn. As this physiological fall-and-rise during day and night may provide an explanation in isolated cases of patients where the clinical assessment is discordant with biochemical results, awareness of the presence of a physiological rhythm is important among individuals that interpret concentrations of cTn. This can be achieved via interaction with clinicians and laboratory specialists (e.g. presentations, dialogues, conferences) or via lectures for medicine students of Maastricht University Medical Center. This level of knowledge utilization has already been started through publication of results in the Journal of the American College of Cardiology, a high impact cardiology journal, and through oral presentations at national and international conferences (IFCC, Istanbul, 2014). Additional novel insights arising from future studies will further enhance awareness through publications and presentations. The second step of knowledge utilization is to connect with key-opinion leaders that comprise the writing group on behalf of the joint ESC / ACCF / AHA / WHF Task Force for the Universal Definition of Myocardial Infarction.[3] This level of knowledge transfer has been initiated by the collaboration with the research group of Prof. dr. Mueller (University Hospital Basel, Switzerland), a senior scientist behind major breakthroughs related to the optimal diagnostic algorithm of cTn for the diagnosis of AMI. The final step is the actual integration of the diurnal rhythm into guidelines such as the expert consensus document 'Universal definition of myocardial infarction'.[3]

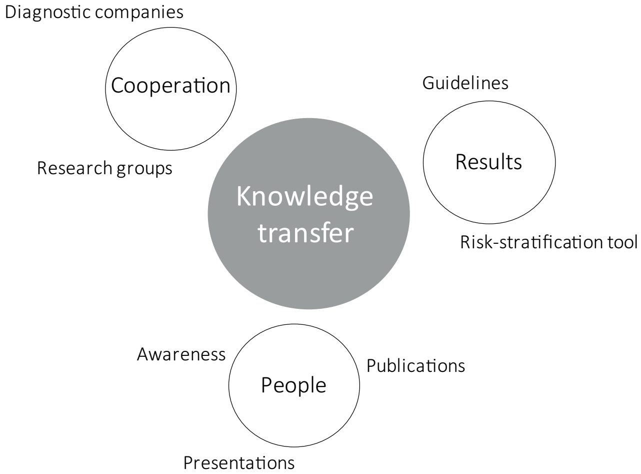

Figure 1. Potential knowledge transfer activities based on the research findings described in this thesis.

Results of this thesis support the concept that cTn can be implemented into risk-stratification scores to identify individuals in the general population at risk for cardiovascular diseases. The national guideline for general practitioners recommends to determine the risk and need for prevention consultation for patients according to a medical risk questionnaire, without the measurement of biomarkers.[13] To initiate the first step of knowledge utilization (awareness), future studies should aim to determine the additional value of cTn concentrations in this risk calculation tool used by general practitioners.

The research findings concerning exercise-induced cTn release have the potential to be utilized by (recreational) athletes. The first step would be to organize information meetings and discuss the effects of endurance-type exercise. To initiate this first step of valorization, more studies are needed to make a definite statement regarding the underlying process (i.e. physiological or pathological) of exercise-induced cTn release.

Troponin testing involves the measurement of one of two proteins – cardiac troponin T (cTnT) or I (cTnI) – with distinct biochemical properties, but comparable diagnostic performance.[14] A recent European survey demonstrated that 50% of the inquired laboratories use cTnT and 45% use cTnI concentrations as part of the diagnostic workup for AMI.[15] This thesis described minor differences between cTnT and cTnI in terms of their diurnal variation and prognostic value. Future studies should aim to compare cTnT and cTnI measured by hs assays across the broad spectrum of cardiovascular disease. Awareness of these comparisons among the individuals that interpret cTn concentrations have the potential to result in a pathophysiological preference of one troponin biomarker over another and could influence the troponin test offered by the clinical laboratory.

cTn are already incorporated into clinical practice. Therefore, research focusing on the biomarker has the potential for cooperation with diagnostic companies regarding for example the implementation and evaluation of troponin assays. The first level in this knowledge transfer activity has already been initiated, as the Central Diagnostic Laboratory of Maastricht has excellent collaborations with Roche Diagnostics, Abbott Diagnostics and Beckman Coulter.

Conclusion

Research findings of this thesis can be translated into several knowledge transfer activities involving people, results and cooperation. Although the outcomes of these mechanisms of knowledge utilization are different, the first step, i.e. creating awareness through publications or presentations, is identical among all knowledge utilization activities.

References

1. VSNU. Een Raamwerk Valorisatie-indicatoren. www.vsnu.nl/valorisatie2013.
2. Finne H, Day A, Piccaluga A, Spithoven A, Walter P, Wellen D. A Composite Indicator for Knowledge Transfer. 2011.
3. Thygesen K, Alpert JS, Jaffe AS, et al. Third universal definition of myocardial infarction. Eur Heart J. 2012;33(20):2551-2567.
4. Centraal Bureau voor de Statisiek. StatLine. statline.cbs.nl.
5. RIVM. Kosten van Ziekten. www.kostenvanziektentool.volksgezondheidenzorg.info.
6. Nawar EW, Niska RW, Xu J. National Hospital Ambulatory Medical Care Survey: 2005 emergency department summary. Adv Data. 2007(386):1-32.
7. Mueller C. Biomarkers and acute coronary syndromes: an update. Eur Heart J. 2014;35(9):552-556.
8. Wiese M. Reducing short-stay hospital admissions by ruling out non-ST elevation myocardial infarction and estimating coronary artery disease likelihood on an emergency department observation ward. BMJ Qual Improv Report. 2013;2.
9. Reichlin T, Hochholzer W, Bassetti S, et al. Early diagnosis of myocardial infarction with sensitive cardiac troponin assays. N Engl J Med. 2009;361(9):858-867.
10. Giannitsis E, Katus HA. Cardiac troponin level elevations not related to acute coronary syndromes. Nat Rev Cardiol. 2013;10(11):623-634.
11. de Lemos JA, Drazner MH, Omland T, et al. Association of troponin T detected with a highly sensitive assay and cardiac structure and mortality risk in the general population. JAMA. 2010;304(22):2503-2512.
12. Khot UN, Khot MB, Bajzer CT, et al. Prevalence of conventional risk factors in patients with coronary heart disease. JAMA. 2003;290(7):898-904.
13. NHG. NHG-standaard Het PreventieConsult. www.nhg.org/standaarden.
14. Rubini Gimenez M, Twerenbold R, Reichlin T, et al. Direct comparison of high-sensitivity-cardiac troponin I vs. T for the early diagnosis of acute myocardial infarction. Eur Heart J. 2014;35(34):2303-2311.
15. Pulkki K, Suvisaari J, Collinson P, et al. A pilot survey of the use and implementation of cardiac markers in acute coronary syndrome and heart failure across Europe. The CARdiac MArker Guideline Uptake in Europe (CARMAGUE) study. Clin Chem Lab Med. 2009;47(2):227-234.