Perspective

Patient safety and risk management in medical laboratories: theory and practical application

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Abstract: Patient safety, defined by the Institute of Medicine (IOM) as "the prevention of harm to patients", is the ultimate goal of medical laboratory services. Although it has been demonstrated that the error rate in medical laboratories is very low compared to the billions of tests daily performed, and that most of these errors rarely become unfavourable events, adverse outcome may occur and may also become the object of daily news. Risk management principles should therefore be considered as integral parts of laboratory in assuring quality and safety, so that they have become actual requirements (4.14.6) of International Organization for Standardization (ISO) 15189:2012, the international standard for accreditation of medical laboratories. Risk is no longer thought in negative sense, but becomes a tool to identify improvement opportunities and preventing negative outcomes. ISO/TS 22367 and some Clinical and Laboratory Standards Institute (CLSI) guidelines (i.e., EP18-A2 and EP23-A) introduce risk management principles and they can be used for driving application of ISO 15189 as a system for reducing laboratory error and improving patient safety. Laboratory goals, organization within which the laboratory operates along with available resources, are all key elements for selecting the technique to be used for risk assessment. However, although different approaches have been suggested, failure modes and effects analysis (FMEA) is the most commonly applied. There are currently few reports on active use of risk management tools in medical laboratories. Some of these are limited to risk identification and estimation steps, whilst others report corrective measures without verifying their effectiveness. Risk management, however, is a process consisting of three main phases (i.e., risk identification, estimation and control), and should hence embrace all its phases to achieve its goal, that is ensuring patient safety. This paper summarizes the principles of risk management process applied to clinical laboratory and discusses some practical applications available in the literature.

Keywords: Risk management; patient safety; International Organization for Standardization 15189 (ISO 15189); errors; failure modes and effects analysis (FMEA)

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Patient safety: the goal of medical laboratories

Patient safety is defined as the absence of avoidable patient harm due to adverse events occurring in any process of medical attention. Nevertheless, adverse events may still occur and also become the object of daily news. After several decades during which healthcare professionals have denied the existence of medical errors, the report "*To error is human*: *Building a Safer Health System*" published in 1999 has changed the idea of healthcare quality worldwide, raising awareness that medical errors may have a large impact on patients (1).

Unlike other specialities, such as emergency and intensive care medicine, laboratory medicine is considered a low-risk speciality (2). Two main aspects contribute to this consideration. On the one hand, the fact that the main

activities in laboratory medicine are precisely defined (3,4) and are so considered more controllable than a procedure in an emergency department, which is strictly dependent on healthcare professionals. On the other hand, the result of a laboratory error that could either directly or indirectly affect patients can only be identified at the end of the entire healthcare process. In the most of cases, however, laboratory services represent the first step of the clinical decision-making, providing essential information influencing nearly 70% of diagnoses and subsequent patient management (5).

In this context, and assuming that any error occurring in the testing process may impact the accuracy of laboratory data and harm patient, several strategies for reporting, monitoring and analysing laboratory errors have emerged since the 2000s (6). These strategies, in addition to automation, information technologies, improved laboratory technology and assay standardization, have contributed to reduce the prevalence of errors, initially at analytical steps, and more generally in the entire laboratory process (7). Although it has been shown that: (I) the error rate in medical laboratories is very low (one error identified every 330–1,000 events, meaning every 900–2,074 patients or 214–8,316 laboratory results) (2); and (II) the majority of these error rarely become adverse events (8), patient safety should be considered the goal of laboratory services and its principles must be systematically applied in a well-structured manner.

Although errors are generally attributed to failures of healthcare staff, most of them result from failure to design safe processes. The laboratory director is hence now in charge of creating a safer medical laboratory. In the patient-centered laboratory, it is no longer enough to identify, analyse and monitor errors, but it is now compelling to understand and manage the potential risks error associated with errors. The "Clinical Risk Management", described as the systematic process for identifying and managing the actual and potential risks associated with laboratory testing (9), is becoming an integral part of organizational culture, a key component of quality management system and plays an important role in ensuring quality services.

The risk management in the medical laboratories

From risk to opportunities

The concept of risk management, regularly used in aerospace and automotive industries since the 1960s (10), has been initially applied to medical laboratories by the *in vitro* diagnostic manufacturers, in which products and components are subjected to stringent risk assessments before being marketed. Accredited medical laboratories, however, are now forced to implement risk management principles.

Although implicit in the International Standard for medical laboratories accreditation, the International Organization for Standardization (ISO) 15189:2007 (11), the concept of risk became explicit and patient-centered only in the 2012 revision (12). Searching for "risk" in the 2007 version of the Standard, the term appears twice, at 4.10 (corrective actions) and 5.2 (accommodation and environmental conditions) points (11). The term was used to promote the reactive approach, focused on events ("*Corrective action should be appropriated to the magnitude of the problem and commensurate with possible risk*") and to minimize the accommodation and occupational risks ("*The laboratory shall be designed for the efficiency of its operation, to optimize the comfort of the occupants and to minimize the risk of injury and occupational illness. Patients, employees and visitors should be protected from recognized hazards*") respectively. In the 2012 review (12), the term "risk" is used as many as 6 times (4.11, 4.12, 4.14.6, 4.13, 4.15.2, 5.6.2.2). It appears no longer in corrective actions but in preventive actions (4.11) and continual improvement (4.12) chapters, thus stemming for application of a proactive approach, focused on processes rather than events, and ultimately promoting the culture of prevention and continual improvement. Risk is no longer thought in negative sense, but as a process for identifying opportunities ("*Preventive action is a proactive process for identifying opportunities for improvement rather than a reaction to the identification of problems or complaints*"). Any error might indicate weaknesses in policies and procedures that may not lead to adverse events in such particular context, but might cause patient harm in slightly different circumstances.

Moreover, for the first time risk management appears as an actual requirement (4.14.6) applied to medical laboratories ("*The laboratory shall evaluate the impact of work processes and potential failures on examination results as they affect patient safety, and shall modify processes to reduce or eliminate the identified risks and document decisions and action taken*"), underlining the change in healthcare professional culture, from error detection to management of risk throughout all steps of laboratory medicine.

The risk management process: the theory

Although the introduction of risk management as a requirement places a new focus on medical laboratories, the Standard does not specify the methodology to apply. Laboratory professional are therefore asked to understand the principles of risk management and choose the best methodology. To this end, the ISO 31000 "Risk management—Principles and guidelines" (13), may be a useful reference, although it is not specific for medical laboratories like the majority of available standard and guidelines on risk management, which have been mostly geared toward manufacturers. The technical specification ISO/TS 22367 "Medical laboratories—Reduction of error through risk management and continual improvement" (14) and two Clinical and Laboratory Standards Institute (CLSI) guidelines EP18-A2 "Risk management techniques to identify and control error sources" (15) and EP23-A "Laboratory quality control based on risk management" (16), now introduce risk management into clinical laboratory and can be used to guide the application of ISO 15189 as a system for reducing laboratory error and improving patient safety.

According to ISO 73:2010 "Risk management-Vocabulary", risk management is defined as "*the systematic application of policies, procedures and management practices in the activities of communication, consultation, in establishing the context and also to identify, to analyze, to assess, to treat, to monitor and correct the risk*" (17). It is hence described as a global process, which should anticipate what may go wrong (non-conformities, errors and accidents), thus assessing plausibility of errors occurrence along with consequences they cause and implementing strategies to reduce the risk of potential harm. Since there is no zero-risk activity, the ultimate goal of this process is to reduce the risk to an acceptable level for both patients and clinicians.

The spectrum of risks is broad, and ranges from very low risk to very high. An empirical equation links with an inverse relationship the severity of an event and its occurrence probability, so that frequent events with a low level of severity are potentially high-risk events, whilst isolated events with high level of severity are very high-risk events. The first step of the risk management process concerns then the systematic identification of risks associated with the total testing process. Since risk is defined as "*the effect of uncertainty on the achievements*" (17), this step must be related to laboratory's goals. The organization within which the laboratory operates and the available resources are other factors to be considered when choosing approaches. From patient safety perspective, all hazard situations in the laboratory should be analysed before harming patients. According to this principle, the CLSI EP18-A2 document proposes a proactive tool, failure modes and effects analysis (FMEA), to identify *potential* sources of errors, establish how they could affect the processes under investigation, and implement control measures to detect and eliminate these errors. Alternately to this bottom-up approach, the CLSI EP18-A2 documents suggests a top-down approach, fault tree analysis (FTA), which starts by assuming a main system failure and determines the root cause of this failure. FMEA and FTA should be alternately or jointly applied to evaluate complex system, before implementing a new test, installing new equipment or introducing any changes to an existing process (15).

Many models have been developed over the past decades to help medical laboratories improving quality (certification and accreditation models, six sigma tool) and enhancing safety (FMEA, hazard and operability studies, probabilistic risk assessment) (6), since complex and mature organizations are now asked to continuously monitor their processes for preventing that *actual* observed failures can be repeated. In this case, the CLSI EP18-A2 document suggests to apply Failure Reporting and Corrective Action System (FRACAS) to all existing laboratory processes. FRACAS is a tool by which failures are identified and analysed, so that corrective actions can be implemented (15).

Once identified, potential either actual failures, their risk must be estimated. According to the ISO 73:2010, which defines the risk as "*a combination between the consequences of an event (including the circumstances changes) and the plausibility of occurrence*" (17), it is necessary to measure the probability of risk occurrence along with the risk severity level. Since many qualitative and semi-quantitative scales for specific healthcare field (e.g., ISO 14971:2007) are available in the literature (18,19), laboratory professionals must choose the most suitable one, according to the level of analysis they are performing and information and data they are willing to obtain. For each failure that can be identified it is possible to obtain a risk priority number (RPN) or a risk code respectively, on whether semi-quantitative or qualitative scale is used. This can be accomplished, by multiplying the probability of risk occurrence and the risk severity level (either interpolating the data on a color-code scale). The risk estimation, also defined risk assessment, is an essential step of risk management process. RPN (or risk code) allows then to distinguishing high from low risk

processes, so prioritizing interventions. Once priorities have been defined, laboratory staff must implement preventive/corrective actions for maintaining the risk within an acceptable level. However, as demonstrated by Lao and colleagues (20), there may be some differences in distribution of failures, and then in interventions prioritization, depending on whether potential risks or actual risks are assessed. These Authors, for example, have shown discrepancies by comparing FRACAS versus FMEA results in pre-analytical and post-analytical phases, but not in analytical steps. Laboratory staff should hence lower the actual failures to an acceptable level, but should be aware and ready to avoid potentially serious risks (but less frequent) that could be masked.

The last step of risk management process, the risk control, involves evaluating the effectiveness of the entire process. The risk should be continuously monitored for verifying that the control measures have been effective, but also for detecting other errors so far overlooked, so finally ensuring patient safety.

From theory to practice

The first application of risk management principles to laboratory medicine, excluding the manufacturing industry, could be attributed to the development of quality control plans. Quality control, in fact, aims to monitor the performance of measuring systems and alert laboratory staff about test errors before impacting patient results. Periodic participation in external quality assurance (EQA) programs is another example of risk management principles applied to medical laboratories (21). These strategies have certainly led to errors reduction in analytical steps so that this phase is now reasonably considered the most well-managed throughout the total testing process. However, as demonstrated by several publications on laboratory-related errors (22-24), the pre- and post-analytical steps are the most errors-prone phases, so that they cannot be ignored as a part of the efforts for improving quality and reducing adverse events. Although there are relatively few reports on active use of risk management tools applied to medical laboratories, the latest ones to be published not only focus on analytical steps (25), but relate to the entire testing process (26-28).

Among the countless techniques for risk assessment (13), laboratory professionals generally apply FMEA (26-29) as recommended by ISO/TS 22367 (14) or other tools suggested by CLSI EP18-A2 (15). In addition, different approaches are used to defining goals and identifying risks. Lao and colleagues (20), for example, mapped the total testing process by using a Visio Standard 2007 Microsoft Office program in order to obtain a global perspective of laboratory. The potential and actual failures modes associated not only with operational (pre-analytical, analytical and post-analytical), but also to strategic and support processes, have been identified by analysing literature data. The risks estimation has shown that strategic and support processes, due to their lower estimated frequency and gravity, respectively, contribute to patient risk rate much lower than the operational processes. Depending on whether potential risks or actual risks are assessed, high priority risks could be related to pre-analytical and post-analytical steps, respectively. These discrepancies are due to the different tools used. While FMEA has allowed estimating the potential risks on considering severity, frequency and detection, FRACAS did not include detection in the calculation of actual risks.

Serafini and colleagues (27) chose to analyse the entire testing process of a specific test, the Factor V Leiden mutation, since the high variability of this test is responsible for wrong results with a consequent number of repetitions and incremental costs. Applying the failure mode, effects and criticality analysis (FMECA) tool, the authors identified 51 activities, 23 of which showed an acceptable risk level (RPN <100), whilst 8 needed corrective actions (100< RPN <150) and the remaining drastic and timely preventive actions (RPN >150). The activity that measured the highest RPN was a post-post-analytical activity, i.e., results interpretation. Two considerations may be brought to explain this data: (I) an error has a negative impact on patient as shortest is the time between one process and another, due to the limited number of barriers useful to intercept and eliminate errors; (II) more the completion of a process entails human (physical and intellectual) intervention, more likely the increase of the harm.

Magnezi *et al.* (28) also applied the FMEA technique to reduce the multiple failures recorded in specific testing procedures (i.e., parathyroid and adrenocorticotropic hormones tests). According to FMEA analysis conducted by Lao *et al.* (20), the four failure modes with a higher RPN ranking (the courier delayed on the way to the laboratory; the tube was not refrigerated; the courier did not arrive in a reasonable time; the sample was sent via the pneumatic system without refrigeration) concerned pre-analytical activities. In addition, the analysis of root causes showed that failures are due to non-laboratory personnel, according

to other studies available in literature (30-34), thus emphasizing that errors are often the result of a poor system design leading to problems in communication, integration of services and lack of accountability for areas where one service ends and another begins.

The FMEA principles were instead specifically applied to pre-analytical phase by Flegar-Meštrić *et al.* (29). In this study, failures mode identification and risks estimation were possible by using data, retrospectively collected, from 22 harmonized quality indicators (QIs) of the model of quality indicators (MQI) launched by the International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) Working Group on "Laboratory Errors and Patient Safety" (WG-LEPS) and covering all steps of the pre-analytical process (35,36). The authors identified five failures, all related to suitability of sample and corrective actions. The reduction of RPN after three months from implementation of corrective actions showed their effectiveness summed to that of the entire risk management process, although FMEA remains a technique especially useful for evaluating a new process prior to its implementation and not for process monitoring. This is one of the few studies in which the risk management process has been conducted in its all phases, from risk identification to risk control. Several studies were in fact limited to risk identification and assessment (28,37), whist others reported the corrective measures without verifying their effectiveness in terms of RPN reduction (27).

Any actual or potential error that may impact patient safety must be managed. As demonstrated by other authors (38), errors monitoring does not automatically result in quality improvement. Detecting and managing errors to avoid negative outcomes should be conducted with a systematic approach, focused on systems design failure rather than human failure. For this reason, the Australasian QIs program Key Incident Monitoring and Management System (KIMMS) has encouraged laboratories to be aware of the risk errors-associated and to explore the causes of such errors. Participants laboratories, in addition to other statistics, receive the RPN calculation. For each QIs, the system automatically multiplies the three variables: (I) frequency imputed by lab participants; (II) harm; and (III) detection previously defined through a lab professional consensus resulted in a KIMMS risk matrix. The system also requires reporting the area (inside or outside laboratory), source and detection system (compliant, laboratory quality system, unknown) of errors, in order to encourage participants to analyse the causes and responsibility of these errors (39). Detection, identification and monitoring of errors through a set of harmonized, evidence-based and patient-centred QIs, are effective tools for risk assessment. QIs incorporated in laboratory quality management system can minimize the possibility of errors occurrence and, consequently, enhance patient safety.

Conclusions

The Institute of Medicine (IOM) considers patient safety "*indistinguishable from the delivery of quality health care*" and defined it as "*the prevention of harm to patients*" (1). Quality in healthcare appears as strictly connected to risk management principles. On the basis of this assumption, full implementation of risk management and quality management systems should not be regarded as separate activities, but should be integrated within everyday practice of all laboratory professionals. Thus, moving from a focus on human failures (e.g., by systematically applying risk management principles and implementing evidence-based practice to tackling system failures) and improving the quality of care can be considered the best solution to improve patient safety.

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