Kontrola kvalitete u laboratorijskoj dijagnostici iz nove perspektive

Total quality in laboratory diagnostics. It's time to think outside the box

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Laboratorijska dijagnostika je područje koje se brzo razvija, što značajno doprinosi donošenju kliničkih odluka u prevenciji, postavljanju dijagnoze i terapijskom praćenju većine, ako ne i svih bolesti (1). Kvaliteta i sigurnost dijagnostičkih analiza od ključne je važnosti u promicanju cilja visoko-kvalitetne i sigurne zdravstvene zaštite. Niti jedna druga disciplina nema tako prominentnu poziciju u pružanju rješenja o sigurnosti bolesnika, kao što to ima laboratorijska medicina (2). Iako postoji klasična podjela cjelokupnog procesa laboratorijskog rada na tri pojedinačna, no uzastopna područja (prijeanalitička, analitička i poslijeanalitička faza), velik broj dokaza ukazuje na činjenicu da se velika većina pogrešaka događa u izvananalitičkim područjima rada, posebice kod prijeanalitičkih neautomatiziranih postupaka (3-7). Prijeanalitička faza predstavlja najkritičnije područje u procesu postizanja napretka u ukupnoj kvaliteti laboratorijske dijagnostike.

U ovom broju časopisa objavljujemo zanimljivo presječno anketno istraživanje o učestalosti pojedinih postupaka izvananalitičke faze laboratorijske dijagnostike u Hrvatskoj (8). Rezultati su sakupljeni od 144 člana Hrvatske komore medicinskih biokemičara (HKMB) anonimnim upitnikom od 20 pitanja po principu Likartove ljestvice kojim se ispitivala učestalost prijeanalitičkih postupaka. Pitanja su bila podijeljena u tri skupine (kriteriji za prihvaćanje uzorka, postupci uzorkovanja krvi, izvještavanje o nalazima) iz kojih se izračunao prosječni rezultat za svaku skupinu. Ukupni prosječni rezultat bio je globalno zadovoljavajući te nije primijećena razlika vezana za tip laboratorijske ustanove, stupanj stručnog obrazovanja ili informatičkih vještina. Rezultat postupka uzorkovanja krvi bio je najslabije ocijenjen te je poražavajuće priznanje gotovo četvrtine ispitanika da nisu nikada ili su u rijetkim slučajevima prijavili nesukladnosti u svom laboratoriju. Rezultat skupine pitanja koja je obrađivala kriterije za prihvaćanje uzo-

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Laboratory diagnostics is a fast-growing field, which provides a substantial contribution to the clinical decision making by supporting prevention, diagnosis, and therapeutic monitoring of most, if not all, human disorder (1). Quality and safety in diagnostic testing is, however, essential to furthering the goal of high-quality and safe healthcare, no other disciplines having such a prominent position in the patient safety solution than laboratory medicine (2). Whereas the total testing process is classically divided into three separate but sequential areas (i.e., preanalytical, analytical and postanalytical phases), a large body of evidence attests that most errors occur within the extra-analytical areas of testing, especially in the manually intensive preanalytical processes (3-7). As such, the preanalytical phase actually represents the most critical area to target for achieving major improvements in the total quality of laboratory diagnostics.

In this issue of *Biochemia Medica*, we publish an interesting cross-sectional survey study on self reported routines and procedures for the extra-analytical phase of laboratory practice in Croatia (8). Results were collected from 144 members of Croatian Chamber of Medical Biochemists (CCMB) using anonymous questionnaire with 20 Likert scaled questions testing self-reported frequency of preanalytical procedures. Questions were also divided in three groups (criteria of acceptance of sample, procedures of phlebotomy, test results reporting), which average score was calculated accordingly. The average overall score was globally satisfactory and no differences could be observed concerning the type of laboratory institution, professional degree or computer skills. The procedures of phlebotomy score achieved however, the lowest score and, disappointingly, nearly one fourth of the participants reported to never or rarely record nonconformities in their laboratories. The criteria of sample accep-

raka bio je također značajno niži među magistrima medicinske biokemije, nego među laboratorijskim stručnjacima sa specijalizacijom iz medicinske biokemije. Jedno od saznanja do kojeg se došlo jest da je osoblje privatnih laboratorija očigledno više usredotočeno na odgovarajuće postupke uzorkovanja krvi. To se može logički objasniti postojanjem konkurencije kojoj su privatni laboratoriji izloženi na otvorenom tržištu pa je nužna povećana pažnja oko uzorkovanja krvi kako bi se spriječile pritužbe bolesnika.

Ovi nam rezultati jasno pokazuju potrebu za pojačanim aktivnostima za poboljšanje izvananalitičkih postupaka laboratorijskog rada, posebice kod prikupljanja bioloških uzoraka.

Slično nacionalno istraživanje pod pokroviteljstvom Talijanskog društva kliničke biokemije i molekularne biologije (SIBioC) i Talijanskog društva laboratorijske medicine (SIMeL) provedeno je 2006. godine i dalo je gotovo identične rezultate. Analiza podataka otkrila je visok stupanj varijabilnosti između laboratorija za većinu prijeanalitičkih postupaka (npr. uzorkovanje kod ambulantnih bolesnika, transport uzoraka). U to je vrijeme samo 31% laboratorija imalo automatizirane neke prijeanalitičke korake, a njih 19% nije imalo standardne protokole za transport uzoraka. Period skladištenja i uvjeti ponovnog testiranja su također bili vrlo heterogeni. Sukladno rezultatima istraživanja HKMB, samo 63% laboratorija uklopilo je kodirane postupke za upravljanje nesukladnim uzorcima (9). U usporedbi s talijanskim iskustvom, gdje je i razvijen upitnik kako bi se dobili kategorički odgovori (npr. da ili ne), velika prednost istraživanja objavljenog u ovom broju je metodološki pristup temeljen na Likertovoj ljestvici koja predstavlja najčešće korištenu psihometrijsku ljestvicu u istraživanjima koja se temelje na upitnicima (10). Prilikom odgovaranja na pitanje oblikovano po principu Likertove ljestvice, ispitanik mora specificirati stupanj svog slaganja s određenom izjavom pomoću stupnjevitih odgovora („nikada", „rijetko", „često" i „uvijek") čime se dobivanju ordinalni podaci koji omogućuju izračun pouzdanog rezultata za svaku skupinu pitanja.

Laboratorijski stručnjaci, regulatorna tijela i dijagnostička industrija već su desetljećima usredotočeni na kvalitetu analitičkog rada. Iako još uvijek nije oslobođena pogrešaka, analitička faza laboratorijske analize je pod strogom kontrolom primjenom materijala Međunarodne kontrole kvalitete (engl. *Internal Quality Control*, IQC), programa Vanjske procjene kvalitete rada medicinsko-biokemijskog laboratorija (MBL) (engl. *External Quality Assessment*, EQA) i izračunima mjerne nesigurnosti (2,11,12). Neovisno o raširenosti svijesti o ozbiljnim problemima koji bi mogli nastati u izvananalitičkoj fazi laboratorijske analize, malo je poduzeto kako bi se smanjila nesigurnost koja dolazi s tog područja. Došlo je vrijeme da se laboratorijski rad sagleda iz nove perspektive, odnosno da se težište postavi na pouzdanije strategije za bolju kontrolu aktivnosti

tance score was also significantly lower among medical biochemists with master degree than in laboratory professionals with a specialization in medical biochemistry. One original finding was that the private laboratories staff is apparently more focused on appropriate blood sampling procedures. This has been reasonably explained with the greater competition which private laboratories are inherently subjected in an open market, where major attention on blood sampling issues is necessary to prevent patient's complains.

These results clearly point out the need for reinforced actions to improve the extra-analytical activities of the testing process, especially for collection of biological samples.

A similar national survey, sponsored by the Italian Society of Clinical Biochemistry and Molecular Biology (SIBioC) and the Italian Society of Laboratory Medicine (SIMeL), was carried out in 2006, and yielded nearly identical results. Data analysis revealed a high degree of variability among laboratories for most preanalytical procedures (e.g., outpatient sampling, sample transportation). Only 31% of laboratories had some preanalytical steps automated at that time and 19% had no standardized protocols for sample transportation. The storage period and conditions for rerun/retest were also highly heterogeneous. In line with the findings of the CCMB survey, only 63% of laboratories had implemented a codified procedure for the management of unsuitable specimens, and half of them had as yet developed a standardized procedure for the management of unsuitable specimens (9). As compared with the Italian experience, where the questionnaire was developed to produce categorical answers (e.g., "yes" or "no"), the great advantage of the study published in *Biochemia Medica* is the methodological approach based on the Likert scale, which is the most widely used psychometric scale in survey research (10). When responding to a Likert questionnaire item, respondents specify their level of agreement to a statement by a graded answer (i.e., "never", "rarely", "often" and "always"), thereby producing ordinal data which enabled the calculation of a reliable score for each group of items.

Laboratory professionals, regulation bodies and the diagnostic industry as well have been focusing for decades on the analytical quality. Although not completely free from errors thus far, the analytical phase of testing is however subjected to a strict control using Internal Quality Control (IQC) materials, External Quality Assessment (EQA) schemes and calculation of measurement uncertainty (2,11,12). Regardless of a widespread awareness of the serious problems that might arise from the extra-analytical phases of testing, little has however been settled for reducing the uncertainty arising from this area. As such, the time has come to think outside the box, to place more focus on reliable strategies for a better control of those activities that inherently lie outside the traditional walls

koje po svojoj prirodi leže izvan kliničkih laboratorija. Iako nije jednostavno definirati polaznu točku, to se mora napraviti. Prvo i osnovno rješenje je prihvaćanje jedinstvene sheme izvještavanja o pogreškama po principu pouzdanih pokazatelja kvalitete za analitičke i izvananalitičke faze laboratorijske analize (13). Projekt „Model pokazatelja kvalitete" koji je nedavno provela radna skupina Laboratorijske pogreške i sigurnost bolesnika (engl. *Laboratory Errors and Patient Safety*, WG-LEPS) koja je aktivna u sklopu Povjerenstva za edukaciju i management (engl. *Education and Management Division*, EDM) unutar Međunarodne federacije za kliničku kemiju i laboratorijsku medicinu *(*engl. *International Federation of Clinical Chemistry and Laboratory Medicine*, IFCC) treba se smatrati dragocjenim temeljem u promicanju i potpori istraživanja pogrešaka u laboratorijskoj medicini, sakupljanju dostupnih podataka o tom problemu i preporučenih strategija i postupaka za poboljšanje sigurnosti bolesnika (14). Budući da procjena kliničkih rezultata s područja laboratorijske dijagnostike predstavlja puno veći izazov od definiranja pouzdanih indikatora kvalitete, sljedeći korak bila bi identifikacija onih laboratorijskih događaja koji se provlače kroz čitav postupak laboratorijske analize i koji su uže povezani s ugrožavanjem sigurnosti bolesnika. Razvoj i primjena pouzdanih i univerzalno prihvaćenih laboratorijskih ključnih događaja prikladni su za ovu svrhu, budući da pružaju nova saznanja o mogućim incidentima. Na ovaj se način povećava odgovornost i pružatelja usluge i njihovih korisnika za sigurnost bolesnika (15,16).

Treći korak ovog važnog procesa je dodatak korisnih koncepata IQC i EQA izvananalitičkim područjima laboratorijske analize (17). To neće biti jednostavan proces, no postoje već neki korisni primjeri koji ukazuju na to da program EQA razvijen za prijeanalitičku fazu može biti ostvariv, praktičan i koristan. U razdoblju od 1998. g. Španjosko društvo medicinskih biokemičara i molekularnih patologa (španj. *Sociedad Española de Bioquímica Clínica y Patología Molecular,* SEQC) razvilo je program EQA za prijeanalitičku fazu koji je usredotočen na analizu razloga odbijanja prijema uzoraka. Program se provodi u dva ciklusa godišnje. Od sudionika se traži da zabilježe odbijanja i razloge odbijanja rutinskih ili hitnih uzoraka koje obično sakupljaju u svojim laboratorijima. Podaci sakupljeni kroz 10 ciklusa za prijeanalitičku fazu već su analizirani te pokazuju da takav pristup laboratorijima može služiti kao sredstvo lakše kontrole stanja struke i omogućavati im trajno usavršavanje (18). Nedavno je u nekoliko odvojenih kliničkih laboratorija provedena procjena indeksa hemolize, kako bi se ispitala provedivost uspostave programa EQA za upravljanje hemolitičnim uzorcima. Referentni serumi s različitom količinom hemolizirane krvi i koncentracijom slobodnog hemoglobina od 0-2,0 g/L distribuirani su u sedam odvojenih kliničkih laboratorija u Europi. Indeks hemolize određen je u triplikatu na sedam automatiziranih sistema za kliničku kemiju. Zanimljivo je da je primijećena zado-

of the clinical laboratories. Although we all know that this is not simple, a starting point must be established. A first and foremost solution is the adoption of uniform reporting schemes for error events based on reliable quality indicators for both the analytical and extra-analytical phases of testing (13). As such, the recent project "Model of Quality Indicator", undertaken by the Working Group, "Laboratory Errors and Patient Safety (WG-LEPS)" instituted by the division of Education and Management (EMD) of the International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) must be regarded as a valuable foundation to promote and encourage investigations into errors in laboratory medicine, collect data available on this issue and recommend strategies and procedures for improving patient safety (14). Since the assessment of clinical outcomes in relation to laboratory diagnostics is even more challenging than establishing reliable quality indicators, the next step is the identification of those laboratory events arising transversally across the entire testing process that are more closely associated to a tangible harm for the patient. The development and implementation of reliable and universally agreed-upon laboratory "sentinel events" is thereby suited for this purpose, since it would allow to gain new knowledge about incidents and hold both providers and stakeholders accountable for patient safety (15,16).

The third step of this important process is the extension of the valuable concepts of IQC and EQA to the extra-analytical areas of testing (17). Although this will not be simple, there are already some valuable examples that an EQA program developed around the preanalytical phase might be feasible, practical and useful. Since the 1998, the Sociedad Española de Bioquímica Clínica y Patología Molecular (SEQC) has developed an EQA program for the preanalytical phase, focused on the analysis of causes for rejection of samples usually collected in laboratories and including two cycles per year. The participants are asked to register rejections and causes for rejection of routine or stat samples usually and locally collected at their laboratories. Data gathered throughout 10 blood cycles for the preanalytical phase have also been analyzed already, demonstrating that this approach might provide laboratories with a useful tool for an easier follow-up of their state-of-the-art and, incidentally, allowing them to implement continuous improvement (18). Most recently, a multicenter evaluation of the hemolysis index has been carried out to investigate the feasibility of establishing an EQA for managing hemolytic specimens in separate clinical laboratories. Reference sera containing varying amounts of hemolyzed blood and containing free hemoglobin contaminations ranging from 0 to 2.0 g/L were shipped to seven separate laboratories across Europe. The hemolysis index was then tested in triplicate on seven automated clinical chemistry systems. Interestingly,

voljavajuća podudarnost rezultata između različitih analitičkih platformi, a nesuglasnosti su značajno smanjene nakon normalizacije rezultata prema graničnim vrijednostima svakog instrumenta (19). Ti rezultati nadalje podržavaju korisnost programa EQA za procjenu i promatranje sustava kvalitete kliničkih laboratorija u cijelosti (20). Nadolazeći razvoj i uvođenje nacionalnih programa EQA u Hrvatskoj za izvananalitička područja laboratorijskog rada trebao bi se stoga shvatiti kao velika prilika za poboljšanje kvalitete čitavog postupka laboratorijske analize, pogotovo jer su postupci izvananalitičke faze puno osjetljiviji. To bi moglo biti od ključne važnosti za prepoznavanje kritičnih točaka u laboratorijskom radu i sustavno promatranje svih laboratorijskih procesa s ciljem pripreme za administrativno zahtjevan proces akreditacije (21).

Prošlih je godina primijećen značajan napredak u shvaćanju važnosti sigurnosti bolesnika i potreba smanjenja broja pogrešaka koje se mogu spriječiti. Laboratorijska medicina popločava taj put velikim brojem projekata u cijelom svijetu. Budući da primarne prepreke više nisu tehničke prirode, sigurnost bolesnika zahtjeva višeslojan pristup koji obuhvaća potpunu kontrolu laboratorijskog rada, od uputnice do nalaza. Došlo je vrijeme da se laboratorijski rad sagleda iz nove perspektive te da se pažnja usmjeri na izvananalitičke procese koji su podložniji pogreškama.

a satisfactory agreement of results was observed among the various analytical platforms and the discrepancies were remarkably attenuated after normalizing results according to the instrument-specific alert value (19). These results further support the usefulness of EQA programs for assessing and monitoring the total quality systems of clinical laboratories (20). The forthcoming development and introduction of a national EQA scheme in Croatia for the extra-analytical areas of testing must therefore be regarded as a great opportunity to improve the quality of the total testing process, inasmuch as those processes falling outside the analytical phase are much more vulnerable. This might be crucial for identifying critical points in laboratory activity and to systematically monitor all laboratory processes to prepare for the administratively demanding process of accreditation (21).

Recent years have seen a significant improvement in perceiving the importance of patient safety and the need to reduce the burden of preventable errors. Laboratory medicine is paving the way throughout a series of projects worldwide. Given that the primary obstacles are no longer technical, patient safety requires however a multifaceted approaches, encompassing total control of activities, from test request to results reporting. As such the time has come to think outside our traditional laboratory "box", and target those extra-analytical processes that are more vulnerable to errors.

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