53° Congresso Nazionale della Società Italiana di Biochimica Clinica e Biologia Molecolare Clinica (SIBioC - Medicina di Laboratorio)

Vertual Edition, 11-13 ottobre 2021

Riassunti Sessioni Scientifiche

Codice Abstract	Titolo Sessione Scientifica
• **SS01-01, SS01-02, SS01-03, SS01-04**	Problematiche extra-analitiche nella diagnostica decentrata
• **SS02-01, SS02-CO01, SS02-CO02**	Il monitoraggio delle terapie anticoagulanti orali durante la pandemia da COVID-19
• **SS03-01, SS03-02 SS03-03**	Medicina di Laboratorio di prossimità e telemedicina nella malattia diabetica: innovazione tecnologica e nuove prospettive
• **SS04-01, SS04-02 SS04-03, SS04-CO03 SS04-CO04**	Diagnostica ematologica decentrata
• **SS05-01, SS05-02**	Cure primarie, poct e prove di efficacia: la sinergia necessaria
• **SS06-01, SS06-02, SS06-CO05, SS06-CO06**	Big data e valutazione dei risultati prodotti della diagnostica di laboratorio nei percorsi di cura dei pazienti territoriali
• **SS07-01**	La diagnostica molecolare decentrata: “rischi e opportunità”
• **SS08-CO09**	Young Scientists - Evoluzione della Medicina di Laboratorio: strategie e nuove sfide
• **SP01-01, SP01-CO10**	Il ruolo del POCT nella diagnosi delle sindromi coronariche acute
• **SP02-01**	Alleanza per la qualità e miglioramento degli outcome clinici
• **SP03-01, SP03-02 SP03-CO07, SP03-CO08**	Diagnostica decentrata di COVID-19: rischi e opportunità
• **CJ01-CJ03**	Sessione SIBioC Young Scientisis
• **CC01-CC08**	Casi Clinici

Legenda:

SP	Sessione Plenaria
SS	Sessione Parallela
CO	Comunicazione Orale
CC	Casi Clinici
CJ	Sessione Young

Nota dell’Editore: i riassunti sono stati riprodotti senza alcuna revisione dal materiale direttamente fornito dagli autori.

SS01 - Problematiche extra-analitiche nella diagnostica decentrata

SS01-01

THE PREANALYTICAL PHASE IN THE DECENTRALIZED TESTING: DIFFERENCES AND COMPETENCES

G. Bonetti

Laboratory of Clinical Pathology, Esine, Brescia, Italy

Point-of-care testing (POCT) can be used in clinical setting such as hospitals and in areas where decentralized testing is requested (i.e pharmacies, patient homes, healthcare practitioner's office, residences for elderly, blood donation centers, in ambulances, public utility services). ISO 22870:2016, ISO 15189 and Joint Commission indicate that all hospital based POCT must be supervised by the central laboratory; the laboratory director is responsible for standards of performance in all domains of POCT. Decentralized diagnostics are affected by several organizational, environmental, operational and technical challenges. According to CLSI POCT04 (1) nonhospital based POCT programs should have a POCT director who has to develop a process to ensure compliance and implementation of quality testing. The personel responsabilities in nonhospital-based POCT are the same as hospital-based ones. In Italy there isn't a national rule for POCT but different local regional ones. Recently SIBioC WG on POCT produced a recommendation for the use of POCT in hospital setting (2). Laboratory errors may have serious consequences for patient health and outcome. The preanalytical phase is most vulnerable to errors (60-70% of all laboratory errors). Preanalytical errors are quite frequent in decentralized diagnostic because it's usually performed by nonlaboratory personnel or by patients and because the increasing robustness and simplicity of currently available POCT systems can lead to the false perception that no risk or harm to the patient is possible. In CLSI POCT07A the most common preexamination variabiles, potentially source of errors are listed (3). The most common preanalytical errors in decentralized diagnostics are related to patient preparation such as incorrect sampling time, to blood collection as patient identification, to sample handing such as inadequate sample mixing and tube filling, transport and to interferences such as hemolysis. Many constituents have a daily variation and the blood composition undergoes significant changes after food consumption. Sampling should preferably be done after an overnight fast from 7am and 9am and should always be done prior to the potentially interfering diagnostic and terapeutic treatments. If decentralized tests have to be performed at different times it is necessary to record sampling time and time of administration of any therapeutic treatments. For a proper patient identification it is recommended to use barcoding systems. Capillary specimen should be labeled with the patient's first and last name, identification number, date and time of specimen collection, and initials of the person collecting the specimen (4). The recommended order for microcollection is different from venous blood sampling: blood gases (they may be altered if sampling is delayed), EDTA tubes, tubes with other additives and serum tubes (4). Sample clots may cause spurious results, so it's necessary to invert the tubes gently several times. Any anticoagulated sample must be rejected if any detected clot are present. In capillary sampling when blood flow doesn't permit the right sample volume the massage and squeezing around the puncture site may cause falsely decreased concentrations of some analytes due to the dilution of the blood sample with tissue fluid and falsely increased concentration of potassium due to hemolysis. Hemolysis is the most frequent preanalytical error and can affect many assays. Spurious iperkaliemia in whole blood may be found using POCT such as blood gas devices if occult hemolysis is present and no HIL detection system is available.
Most preanalytical errors in decentralized diagnostics can't be detected but can be prevented by standard operating procedures and achieving proper personnel education not only in analytical but also pre and postanalytical phases.

REFERENCES

1 CLSI. Essential Tool for Implementation and management of a Point-of-Care testing program. 3rd ed. CLSI guideline POCT04. Wayne, PA: Clinical and laboratory Standards Institute; 2016.
2. Rampoldi E, Patrucco G, Casati M, Morelli P, Carraro P per il Gruppo di Studio Point of Care Testing (POCT) Implementation and management of the point-of-care testing (POCT): essential indications. Biochim Clin 2021 (ahead of print) DOI: 10.19186/BC_2021.032.
3. CLSI. Quality Management: Approaches to reducing errors at the point of Care: Approved Guideline. CLSI guideline POCT07-A. Wayne, PA: Clinical and laboratory Standards Institute; 2010.
4. CLSI. Procedures and Devices for the Collection of Diagnostic Capillary Blood Specimens; Approved Standard—Sixth Edition. CLSI document GP42-A6. Wayne, PA: Clinical and Laboratory Standards Institute; 2008.

SS01-02

THE PRE-ANALYTICAL PHASE IN THE POCT MANAGEMENT OF TERRITORIAL DIAGNOSTIC NETWORKS

C. Bellini[1], M. Fantacci[2]

[1]Clinical Chemistry Laboratory Analysis, Misericordia Hospital Grosseto, South East Tuscany USL, Italy
[2]POCT Network Director, Valdichiana Amiata Siena-South Laboratory Analysis Director, South East Tuscany USL, Italy

In recent years, the management of territory-based diagnostic networks has taken on a major role, in order to guarantee an effective and efficient service covering the entire territory. Most recently the need for a territorial response to Covid-19 has further highlighted its centrality. In this context the use of point-of-care testing (POCT) represents a valuable diagnostic opportunity that responds to the need for timeliness and proximity for the management of territorial emergencies and urgencies and to support the health activities of zonal hospitals, first-aid points and remote areas. The area of the USL Toscana Sudest is an example of such complexity, both for the extension covering more than 11,000 km2, with a population of about 800,000 inhabitants (density

72/km2), and for its variety, with 60% of municipalities being mountainous or partially mountainous and 1 island municipality. For several years now an ISO 9001:2015 certified territorial POCT Network has been organised to support and integrate laboratory analysis activities, coordinated by the Laboratories, which guarantees a timely and quality diagnostic service close to the places of care and also at domiciliary.
Technological and analytical advances in POCT equipment, together with careful monitoring of Quality Control (QC), have improved the analytical quality of results. However in order to produce an overall quality result and minimise errors that may jeopardise patient safety, the whole process must be addressed for POCT, as we are used to doing for laboratory results. In detail several pre-analytical issues that can cause many potentially harmful errors, also considering the rapid availability of results, are worth focusing. A risk-based approach to POCT management allows to analyse all steps, to set up monitoring indicators to verify their correctness and to implement corrective and preventive measures to decrease the incidence of errors (1). Traceability from request to report and registration of all operators and devices involved (doctor, nurse, patient, request, sample, batch, instrument) facilitate the workflow management and enable verification of data consistency.
Besides the selection of tests (often already preset for the emergency), the timing of their execution useful for the clinical need and the correct preparation of the patient (e.g. fasting), great attention is paid to the procedure for unique identification of the patient and of the biological sample. Also the collection of the sample in terms of type, volume, device and sampling method, and the eventual treatment or storage before analysis are carefully controlled with shared checklists and operating procedures, as well as other QC on the sample, such as for example the presence of bubbles, clots or haemolysis.
It is therefore essential to act on training and to manage the skills of all the operators involved both in the use of the equipment and in its control in presence and remotely. The multidisciplinary committee is crucial in all aspects of the POCT network from the choice of tests, sites and patients, to the supervision of training and competency, as well as in monitoring performances (2).

REFERENCES

1 Brun M, Füzéry AK, Henschke B, Rozak K, Venner AA. Identifying sources of error and selecting quality indicators for point of care testing. Pract Lab Med. 2021 Mar 21;25:e00216. doi: 10.1016/j.plabm.2021.e00216. PMID: 33869709; PMCID: PMC8042172.
2. Nichols JH, Alter D, Chen Y, Isbell TS, Jacobs E, Moore N, Shajani-Yi Z. AACC Guidance Document on Management of Point-of-Care Testing. J Appl Lab Med. 2020 Jul 1;5(4):762-787. doi: 10.1093/jalm/jfaa059. PMID: 32496555.

SS01-03

IL TRASPORTO DEI CAMPIONI BIOLOGICI: ESPERIENZA DELLA REGIONE CAMPANIA

M. D'Amora

Direttore Dipartimento Integrato Medicina di Laboratorio asl Napoli 1 Centro

Il DCA n. 55 del 30.09.2010 ha disposto il "Piano di Riassetto della Rete Laboratoristica Ospedaliera e Territoriale". Con nota prot. 0406752 del 07.09.2020 è stato istituito il Gruppo di lavoro "Rete della Medicina di Laboratorio" per la revisione del citato Piano. Il GDL ha elaborato un documento tecnico ad oggetto "Modalità Trasporto Sangue e Materiali Biologici" che rappresenta la normativa con cui la Campania ha inteso regolamentare tutte le attività relative al trasporto dei campioni biologici per tutte le prestazioni dettagliate nel documento e ne ha definito,per ciascuna,le modalità di organizzazione per garantire una corretta gestione del processo in tutte le sue fasi attraverso la tracciabilità del percorso e nel rispetto delle procedure e protocolli esistenti (Decreto n.219 del 23/06/2021). Il documento evidenzia come tali attività sono necessarie anche per garantire la qualità delle prestazioni e la sicurezza degli operatori. Sinora non esisteva una norma dedicata in Campania. Il documento è stato elaborato con riferimento alle Linee Guida professionali internazionali e nazionali di riferimento e dispone, tra l'altro, che le AASSLL, le AAOO, quelle Universitarie, gli IRCCS ed il privato accreditato, ove esistano modalità difformi da quanto previsto debbano adeguarsi entro sei mesi dall'emanazione. Nell'allegato al decreto sono trattati i seguenti argomenti: 1. Introduzione 2. Definizioni 3. Finalità 4. Norme per il trasporto 5. Modalità Operative 5.1 Confezionamento Campioni Biologici 5.2 Conservazione e Trasporto dei campioni biologici / Raccomandazioni generali 5.3 Conservazione e Trasporto campioni di Biochimica ed Ematologia/Coagulazione 5.4 Conservazione e Trasporto campioni di Tossicologia 5.5 Conservazione e Trasporto campioni di Anatomia Patologica 5.6 Conservazione e Trasporto campioni di Microbiologia e Virologia 5.7 Conservazione e Trasporto campioni biologici per tutte le indagini Genetiche 6. Procedura trasporto materiale biologico all'interno di un presidio sanitario 7. Scheda di Trasporto 8. Fuoriuscita liquidi biologici 9. Tracciabilità 10. Livelli di responsabilità 11. Tabella esami Chimica Clinica ed Ematologia con tempi e modalità di conservazione per singolo test 12. Tabella esami di Microbiologia/Virologia con tempi e modalità di conservazione per singolo test 13 Bibliografia. Le raccomandazioni contenute nel documento si riferiscono ad ogni determinazione che deve essere eseguita con la finalità di procedere nel modo più affidabile per non compromettere l'accuratezza della sua misura dalla fine del prelievo all'inizio dell'analisi, considerando i seguenti elementi: la temperatura di trasporto; l'eventuale necessità di separare il plasma/siero dalla parte corpuscolata; l'eventuale necessità di congelare il campione (previa centrifugazione della relativa provetta);la distanza temporale dalla fase del prelievo. Conclusioni: Il trasporto dei campioni biologici è oggi un tema strategico. La movimentazione di essi non è più un

evento raro ma prassi frequente, sia per la tendenza delle strutture pubbliche agli accentramenti che di quelle private a consorziarsi. Anche il modello hub e spoke ed il fiorire di centri prelievo vede nella movimentazione dei campioni il fulcro delle attività teso a migliorare il servizio ai cittadini. A livello italiano mancano normative univoche per cui diverse regioni hanno disciplinato in materia ed oggi possiamo annoverare fra queste anche la Campania.

SS01-04
POST-ANALYTICAL PHASE IN DECENTRALIZED TESTING

D. Giavarina

Medicina di Laboratorio, AULSS 8 Berica, Vicenza

As with tests in central laboratories, decentralized analyzes show risks of error in the post-analytical phase. Trying to outline some elements of this problem, it is possible to identify at least three critical elements with different peculiarities, with respect to "centralized" analyzes validation, reporting and, last but not least, clinical interpretation of the result.
We can discuss these items with respect to at least three macro areas: the skills of the personnel dedicated to POCT analysis, the available technologies and methodologies, the standardization of procedures.
The validation of the result is the decision to consider an analytical result "valid", reliable, to make decisions. Results from central laboratory are generally considered valid a priori. In the POCT setting, validation is responsibility of personnel performing the test, usually "non-laboratory" people who do not have the training that laboratory professionals do.
Validation of a result must also take into account at least the correctness of the pre-analytical and analytical phases, the devices functionality, as well as the verification of quality through the control systems. Controlling panic and delta check ranges adds further complexity. We can combat these risks of error with continuous training, such as in the pre-analytical and analytical phases; using updated technologies, which allow self-checks, warning systems, blocking of results in case of non-compliance with quality specifications, etc.; using software for self-validation and decision support. We are near the start of Artificial Intelligence and utilizing big data to prove competency of operators, to prove that meters were giving reliable results, close to the other meters in the hospital and to maintain quality control in devices used outside of the hospital and operated by nurses, emergency medical technicians, and others not laboratorians [1].
Numerous studies have shown that reporting can be a critical element, when the execution of the tests is very far from the control of the central laboratory. The example of carrying out tests at pharmacies is emblematic: for some tests, the analytical quality is now sufficient, but there is “an urgent need to adopt recommended decisional levels and reference ranges updated according to the more recently published clinical guidelines [2]. The incorrect laboratory report is the most relevant issue for the post-analytical POCT phase, and specific quality indicators specific quality indicators could be very useful or even mandatory soon [3].
Specific competence counts in the interpretation of the results. For some tests, such as blood gas tests or thromboelastometry, the skills of specialists who have POCT systems at their points of care are likely to be high, often the highest in the health care system. However, there is evidence for others tests and other clinical contexts (monitoring tests [4] or management of critical results [5]) the situation is very variable and sometimes worrying. The training of operators and the assessment of skills must therefore also concern, and with particular attention, the clinical significance of the results and the actions to be taken in the event of critical or unusual results.

REFERENCES

1. Miller JA. https://www.aacc.org/cln/articles/2021/april/artificial-intelligence-is-poised-to-transform-point-of-care-testing (July, 2021)
2. Zaninotto M, Miolo G, Guiotto A, Marton S, Plebani M. Quality performance of laboratory testing in pharmacies: a collaborative evaluation. Clin Chem Lab Med 2016;54:1745-1751.
3. Brun M, Füzéry AK, Henschke B, Rozak K, Venner AA. Identifying sources of error and selecting quality indicators for point of care testing. Pract Lab Med 2021;25:e00216. doi: 10.1016/j.plabm.2021.e00216
4. Choi S, Choi SJ, Jeon BR, Lee YW, Oh J, Lee YK. What We Should Consider in Point of Care Blood Glucose Test; Current Quality Management Status of a Single Institution. Medicina (Kaunas). 2021 Mar 4;57(3):238. doi: 10.3390/medicina57030238. PMID: 33806620; PMCID: PMC8001912.
5. Nichols JH, Alter D, Chen Y, Isbell TS, Jacobs E, Moore N, Shajani-Yi Z. AACC Guidance Document on Management of Point-of-Care Testing. J Appl Lab Med 2020 1;5:762-787.

SS02 - Il monitoraggio delle terapie anticoagulanti orali durante la pandemia da COVID-19

SS02-01
TELEMEDICINE AND HEMOSTASIS-THROMBOSIS CENTRES

D. Barcellona

Dipartimento di Scienze Mediche e Sanità Pubblica Università di Cagliari, SSD di Emostasi e Trombosi Azienda Ospedaliero - Universitaria di Cagliari

Nowadays, telemedicine has different clinical applications since it is used in almost all medical specialties. The COVID-19 pandemic has created not only major economic and social upheavals but also has an important impact on public health. In this emergency situation, the use of telemedicine has been rise aiming to mitigate the effects of COVID-19 on human health (1).
In Italy, the Hemostasis-Thrombosis Centres (HTCs) belong to the Federation of Centres for the diagnosis of thromboembolic disease and the Surveillance of Anticoagulant therapy (FCSA) and they offer the highest possible quality of assistance to patients treated with Vitamin K Antagonists (VKAs) or Direct Oral

Anticoagulants (DOACs).
Unlike DOACs, VKAs need a close monitoring through the Prothrombin Time (PT) expressed as International Normalized Ratio (INR). The test result allows doctors at HTCs to prescribe the correct dosage of VKAs to maintain the INR in the therapeutic range. This means that patients have to go to their HTC more often than patients treated with DOACs.
Telemedicine has been implemented in the routine clinical practice at HTC many years ago (2) and actually, during the COVID-19 pandemic, this system is of significant aid in the management of this therapy allowing patients to perform the test at home or to self-manage their own therapy.
The system is organised as a centralised net-supported program with a server and PC stations in the HTC and workstations in the peripheral districts. Points-of-Care INR allow patients to easy perform the test on capillary blood and to quickly gain the INR result thus reducing the number of controls that patients would perform at the HCT (3). This aspect is of important value during COVID-19 pandemic since overcrowding should be avoided.
In general, self-management and self-testing have similar safety (RR=1.08, 95% CI 0.81-1.45, RR=0.99, 95% CI 0.8-1.23, respectively) than traditional monitoring as reported by the metanalysis of Sharma et al (4). As regard the efficacy, the authors showed a less incidence of thromboembolism when self-management was used (RR=0.51, 95% CI 0.37-0.69) with a trend versus a significant reduction in all-cause mortality (RR=0.68, 95% CI 0.46-1.01) while self-testing allowed to reach a 4.4% (95% CI 1.7-7.18) increase in time in therapeutic range. In accordance with other economic models, the metanalysis also showed that self-monitoring is cost-effective.
Another advantage of the use of telemedicine in HCT is the patients' satisfaction. In our experience (5) 85% of the patients are satisfied with self-testing at home and the quality of life is improved in 87% of them. The cost of test strips was medium–high for 89% of the patients, and 75% of them stated that it was worth improving their quality of life.
Telemedicine is usefull in managing patients on VKAs and, as suggested by the FCSA (6), it is a safe and efficacy system to guarantee an adequate medical assistance not only routinely but especially during pandemic. Finally, telemedicine could be used also for DOACs patients putting in place a system that may allow patients to attach the PDF file of their laboratory tests and to video-call the doctors at HTC.

REFERENCES

1. Doraiswamy S, Abraham A, MD; Mamtani R, Cheema S. Use of Telehealth During the COVID-19 Pandemic: Scoping Review. J Med Internet Res 2020; 22: e24087.
2. Barcellona D, Fenu L, Cornacchini S, Marongiu F. Telemedicine can improve the quality of oral anticoagulation using portable devices and self-testing at home. J Telemed Telecare 2013; 19: 298-301.
3. Sharma P, Scotland G, Cruickshank M, Tassie E, Fraser C, Christopher Burton C et al. Is self-monitoring an effective option for people receiving long-term vitamin K antagonist therapy? A systematic review and economic evaluation. BMJ Open 2015; 5: e007758.
4. Barcellona D, Fenu L, Marongiu F. Point-of-care testing INR: an overview. Clin Chem Lab Med 2017; 55: 800-805.
5. Barcellona D, Mastino D, Marongiu F. Portable coagulometer for vitamin K antagonist monitoring: the patients' point of view. Patient Prefer Adherence 2018; 12: 1521-26.
6. Poli D, Tosetto A, Palareti G, Barcellona D, Ciampa A, Grandone E et al. Managing anticoagulation in the COVID-19 era between lockdown and reopening phases. Intern Emerg Med 2020; 15: 783-86.

SS02-CO01

NEW ORGANIZATIONAL MODEL FOR DECENTRALIZED MANAGEMENT OF ORAL ANTICOAGULANT THERAPY OF ULSS 6 EUGANEA

E. Gnatta, R. Ghirardo, V. Temporin, A.M. Leo

UOC Medicina di Laboratorio Ospedali Riuniti Padova Sud "Madre Teresa di Calcutta" Monselice (Padova-Italy)

Background: Point of Care (POCT) portable coagulometers allow to shift determination of prothrombin time (PT-INR) from central laboratory to peripheral health facilities. In a broad and complex territory such as that of ULSS 6 Euganea, composed of five local health districts with a population of about 936.000 inhabitants, determining PT-INR in territorial decentralized offices is a key objective in therapy control and patient's life quality improvement.
Aim of the study: description of the organizational model for decentralized management of patients in Oral Anticoagulant Therapy (OAT) involving Anticoagulation Clinic (AC), Integrated Home Cares (IHCs) and Routine Medical Cares (RMCs).
Methods: Starting from October 2020, a bidirectional connection was implemented between Laboratory Information System (LIS) of the Ospedali Riuniti Padova Sud "Madre Teresa di Calcutta" Monselice (Padova, Italy) and peripheral offices, where clinical data are collected and PT-INR is determined by POCT portable coagulometers (Coaguchek® Roche Diagnostics, Germany). Information is sent in real time to central laboratory using IT1000 middleware, where data are validated and historicized. Historicized data can be consulted and downloaded like other laboratory exams. Furthermore, for patients followed by AC, data are sent to OAT monitoring software (GESTAOWEB® Tesigroup Milan). Results: the project involved 2980 patients. Centres to which patients are belonging are located throughout the territory of ULSS 6 Euganea and consist of 7 IHCs, 9 RMCs and one AC, a total of 81 POCT instruments for about 60.000 determinations per year. From January 1st 2021 to June 30th 2021 the average frequency of determinations per patient was about 30 days, while the average number of determinations per patient was about 7,5.
Conclusions: the connection with LIS represents project's focal point, allowing historicization of data, making them available at any time for any connected facility. This model simplifies management of both patients in IHC and followed by RMC, allowing easier access to the determination of PT-INR, with more constant therapy control and significant improvement of life quality.

SS02-CO02

THE ORAL ANTICOAGULANT THERAPY CLINICAL MANAGEMENT DURING PANDEMIA: THE SOLUTION FOUND BY THE FCSA 123 HEMOSTASIS AND THROMBOSIS CENTER IN SAVONA

C. Scarone, V. Dovere, C. Traverso, F. Lillo

S.C. Laboratorio di Patologia Clinica ASL 2 Regione Liguria

Background: The emergency caused by the Covid-19 pandemic has forced the reformulation of the operating methods of the Health System, turning the spotlight on the need for greater interaction between hospital and territory. This aspect is even more evident in patients needing for a more strict followup as those under antithrombotic therapy (TAO), making clear the essential usefulness of digital tools and of new organizative models.
Objectives: Minimize the risks for adverse events in patients on oral anticoagulant therapy with vitamin K inhibitor drugs (AVK) or direct oral anticoagulants (DOAC), maintaining an optimal level of clinical / consulting support, allowing accurate monitoring of compliance and managing both hemorrhagic and thrombotic emergencies remotely, in order to reduce access to the Emergency Room (when possible) and to hospital facilities. Methods: The patients in charge at the Thrombosis Center of the San Paolo Hospital in Savona (FCSA 123) are in total 781: 66% diagnosed with atrial fibrillation (FA), 20% for the presence of mechanical or biological valve prostheses and 14% for thrombotic pathologies such as deep vein thrombosis (DV) and pulmonary embolisms (EP). 560 patients are in DOAC, while 221 patients in AVK. During the pandemic, a dedicated mobile telephone number was activated (twelve hours/day from 8 am to 8 pm) equipped with an instant messaging application service. Each patient was asked for an email address and signed consent to the computerized management of TAO therapy and forwarding of health documents. Results: In order to monitor the expected results, the following indicators were evaluated: number of incoming phone calls; number of treatment plans issued for DOAC; time in range for patients in AVK; number of complications recorded in the period under review (April 2020 -April 2021). The results obtained are respectively: about 9000 phone calls received; 560 treatment plans released; time in range from patients in AVK (TTR) 74%; 22 adverse events including two major hemorrhages. Conclusions: The new organization, based on digital support of clinical monitoring, has received high appreciation from patients and consequently a greater compliance with the therapy protocol. This management model has allowed an effective control both of the number and severity of adverse events, while the reduction of outpatient access has allowed to drastically reduce the infectious risk. In addition, e-mailing of reports and treatment plans allowed an optimization of human resources.

SS03 - Medicina di Laboratorio di prossimità e telemedicina nella malattia diabetica: innovazione tecnologica e nuove prospettive

SS03-01

TELEMEDICINA, CURA A DISTANZA E MODELLI DI INTEGRAZIONE CON LA MEDICINA GENERALE

A. Scatena

Direttore UOC Diabetologia, Ospedale San Donato – Arezzo, ASL Toscana Sud Est

La gestione integrata del diabete mellito in Toscana dall'implementazione del Piano Sanitario regionale (PSR) 2008-2010 si basa sulla Medicina d'Iniziativa, che ha lo scopo di intercettare tempestivamente il bisogno di salute prima dell'insorgere della malattia o prima che essa si complichi, rallentandone il decorso e garantendo interventi adeguati e differenziati in rapporto a livello di rischio (proattività). Tale esperienza prevedeva un livello assistenziale di base gestito dai medici di medicina generale e un livello assistenziale complesso gestito dal diabetologo. Con la Delibera regionale nr 650 del 5 Luglio 2016 si amplia la copertura a tutti gli assistiti e si creano PDTA dedicati alle multicronicità con interventi che tengano conto della differente complessità assistenziale; per la prima volta si introduce il concetto di Piano Assistenziale Individuale (PAI) per i pazienti più complessi, gestito dal medico di medicina generale supportato da tutti i membri del team multidisciplinare e multiprofessionale.
Con la legge regionale Toscana n. 20/2020, il PAI diviene la modalità di presa in carica di ogni assistito e deve tenere conto di tutti gli aspetti che incidono sulla salute del paziente, da quelli strettamente sanitari a quelli sociali, e che preveda l'intervento di più professionisti in forme coordinate, quali un Team multiprofessionale. Parallelamente alla legge regionale, la Commissione Permanente per le Attività Diabetologiche della Regione Toscana ha portato avanti la Delibera n 5 del 7 Gennaio 2020 (Percorso diagnostico terapeutico assistenziale per il Diabete nell'adulto. Modello di gestione integrata tra i medici di medicina generale e servizi di diabetologia. Aggiornamento Delibera GRT n. 108/2011- sostituzione del PDTA nell'adulto), nella quale si tracciano le modalità di condivisione del percorso di cura tra medico di medicina generale e specialista diabetologo, a fronte delle variazioni del compenso glicometabolico, delle complicanze acute e croniche e, più in generale, del cambiamento delle condizioni di salute.
I mesi successivi all'emanazione della legge, sono stati caratterizzati dalla pandemia Covid-19, dalla diffusione della telemedicina, grazie anche alla delibera regionale n 604 del 6 Aprile 2020, e con essa al crescere dell'esigenza della condivisione dei dati da parte del team, tanto che nella delibera n 469 del 4 Maggio 2021 si fa riferimento anche ad una software house/piattaforma regionale dedicata. I dati diventano la base per la continua e tempestiva revisione del PAI, utilizzando anche fonti nuove, come i Point of Care (POC) e modalità di assistenza più rapide, come il teleconsulto.
La nostra esperienza con il teleconsulto ha avuto lo scopo di implementare la delibera n5 del 7 Gennaio 2020, migliorare l'appropriatezza prescrittiva e implementare le nuove linee guida farmacologiche. Sono stati inclusi 65 pazienti, per i quali è stato effettuato un

teleconsulto con il medico di medicina generale per discutere le caratteristiche cliniche, il compenso glicometabolico e la classe di rischio cardiovascolare. La terapia è stata quindi adeguata in modo condiviso e sempre con la modalità del teleconsulto è stata gestita e risolta anche la comparsa di effetti collaterali (7,7%) e la programmazione del follow-up.

SS03-02

HOSPITAL AND TERRITORY: PROXIMITY MEDICINE AND THE ROLE OF THE CLINICAL LABORATORY FOR MONITORING THE DIABETIC PATIENT

A. Ognibene

Dipartimento di Medicina di Laboratorio e Trasfusionale USL Toscana Sudest

The Tuscany regional law n. 20/2020, in the preamble, establishes to "guarantee the assisted person the use of an appropriate assistance path in relation to the ascertained needs for health education, preventive services, social assistance, diagnosis, treatment and rehabilitation, where this requires the " intervention of several professionals in coordinated, integrated and programmed forms, the care of the assisted person must take place on the basis of an Individual Care Plan (PAI), which takes into account all the aspects that affect the patient's health, from those strictly health care to social ones, and which provides for the intervention of several professionals in coordinated forms, such as a multi-professional team ". The clinical problem must be recognized and identified promptly in such a way as to require an overall care of the patient by a multi-professional and multidisciplinary team, for clinical framing and / or monitoring. It is necessary to create a permanent link between the professionals involved and in particular between the general practitioner treating the patient, the outpatient specialist and the Laboratory and Diagnostic Service, between which the exchange of information and opinions must be constant, timely and also through the possibilities offered by "Digital Medicine" such as “the teleconsult”, to define the path. The advantages of the multi-professional and multidisciplinary team and of the second-level pathology / specialty outpatient clinic concern all the actors involved: the patient who performs the diagnostic investigations; the General Practitioner (GP) who sees guaranteed the possibility of obtaining an answer to the clinical question or the scheduled management of controls in a short time; and the specialist doctor who uses all the diagnostic potentials present in the hospital or in a multi-specialist outpatient facility, to formulate, in a short time, diagnoses that require multidisciplinary interventions. The clinical laboratory is part of the team as a determining factor both to clarify the clinical question but also to establish the terms and times of 2nd level specialist intervention. The patient with known diabetes accesses the II level of care, exclusively by being sent by the GP using the priority classes as already indicated for the first visit or through a scheduled visit. The use of priority classes for patients in the care of the GP can take place whenever the current situation constitutes a novelty / variation compared to the previous equilibrium, such as to require an assessment in a short time. Different laboratory parameters represent indicators that, introduced in the priority decision algorithm, can, if communicated in a timely manner, define the path and strategies of specialist therapy in the most appropriate way. In the reality of the USL TSE, a project has been developed that allows to communicate via SMS the results of the laboratory parameters, related to diabetes monitoring, to the patient and the GP when these vary significantly compared to previous controls or represent a clinical state that justifies an intervention by the Team.

SS03-03

THE ROLE OF LABORATORY MEDICINE IN THE MANAGEMENT OF MEDICAL DEVICES FOR SELF-MONITORING BLOOD GLUCOSE

M. Carta[1], G. Bonetti[2]

[1]UOC Medina di Laboratorio, Ospedale S. Bortolo, AULSS 8 Berica, Vicenza
[2]Laboratorio Analisi ASST-Valcamonica, Esine

The self-monitoring of blood glucose is of utmost importance for diabetic patients: it allows patients to evaluate their individual response to the therapy and verify whether the glycemic objectives have been met. All of this must of course be based on the use of one data which accurately reflects the glycemia.
The guidelines recommend the use of a device for the self-measurement of glycemia (POCT) which passed the necessary tests of accuracy and precision and thus presents the CE mark. Some studies, however, have emphasized how a non-negligible number of devices bears the CE mark without actually meeting the minimum criteria of accuracy requested (1).
Even the Italian guidelines (2) highlight the necessity that producing firms clearly declare the analytical features of their devices, particularly in terms of accuracy and precision. The hierarchy of the sources of information has the scientific studies of literature in the first place, with the declarations of producers only ranked second. Lacking explicit and comparable references or in the presence of diverging situations around the analytical performances, diabetic facilities may activate a local evaluation of themselves, with a periodic comparison of the accuracy of the devices being recommended anyway.
The evaluation of the accuracy of POCT systems is very discussed. ADA, FDA, CLSI and ISO 195-2013 (only to mention the most authoritative sources) report different targets. The Italian recommendations revolve around the norms ISO 105-2013 which provide that at least 95% of the measures obtained with the glucometer differ of around 0,8 mmol/L with respect to the measurements obtained with the reference method for concentrations < 5.6 mmol/L and of around 15% for concentrations > 5.6 mmol/L. Moreover, at least 99% of the measures must fall between the areas of error A and B displayed in the Clarke error grid (3). According to the FDA, on the other hand, the 95% of the values must not fall beyond 15% from the reference value and the 99% must be within 20%.
In any case, the accuracy of glucometers is based on the comparison with a reference method, and it is thus necessary to utilize a correct reference method in laboratories.
Much has been discussed around possible variables that may alter the quality of a comparative study of this type

(method used, type of capillary or venous sample, use of first or second drop for POCT measurement etc..) but what undoubtedly plays a major role is the use of procedures which can stop the in vitro glycolysis. Traditionally, sodium fluoride (NaF) is used to stop the glycolysis; this, however, is unable to contrast the glycolysis during the first hour of conservation of the sample. The use of inhibitors that associate the NaF with the citrate buffer thus provoking an early inhibition of the glycolysis has proved more effective in that sense.
This aspect has also been recently highlighted from the IFCC Working Group (5) and assessed in some studies. The use of early glycolysis inhibitors (NaF plus citrate) has proved effective to stabilize samples even up to 15 days and this may allow their use even as control material to evaluate the analytical performances of the glucometers alternatively to the materials currently employed which are based on serum or plasma with an addition of glucose and which may present commutability problems.

REFERENCES

1. Pleus S, Baumstark A, Jendrike N, et al. System accuracy evaluation of 18 CE-marked current-generation blood glucose monitoring systems based on EN ISO 15197:2015. BMJ Open Diabetes Res Care. 2020;8(1):e001067. doi:10.1136/bmjdrc-2019-001067.
2. Carta, M., Testa, R. Raccomandazioni per l'autocontrollo della glicemia nel paziente diabetico: sinossi. Riv Ital Med Lab 10, 122–124 (2014). https://doi.org/10.1007/s13631-014-0050-6.
3. International Organization for Standardization. In vitro diagnostic test systems-requirements for blood glucose monitoring systems for self testing in managing diabetes mellitus. ISO 15197:2013.
4. US Food and Drug Administration. Self Monitoring Blood Glucose Test Systems for Over The Counter Use. Guidance for Industry and Food and Drug Administration Staff. Available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/self-monitoring-blood-glucose-test-systems-over-counter-use Document issued September 29, 2020, last accessed June 2021).
5. IFCC Working Group GMECC. How should glucose meters be evaluated for critical care. Available at https://www.ifcc.org/ifcc-education-division/emd-committees/c-poct/wg-gmecc/ (accessed June 2021).

SS04 - Diagnostica ematologica decentrata

SS04-01

ESAME EMOCROMOCITOMETRICO: TELEMEDICINA E COMPETENZE

S. Buoro

Centro di Riferimento Regionale per la Qualità dei Servizi di Medicina di Laboratorio
c/o ASST Grande Ospedale Metropolitano Niguarda, Milano

L'evoluzione tecnologica è un elemento fondamentale della ri-progettazione ed organizzazione dei processi della medicina di laboratorio nell'ineluttabilità dei percorsi di riordino e consolidamento, tuttavia le competenze dello specialista di medicina di laboratorio giocano un ruolo centrale nella governance di questo processo evolutivo.
La diagnostica ematologica nella sua globalità, dall'emocromo, alla caratterizzazione immunofenotipica, genetica e molecolare è uno dei settori della medicina di laboratorio che maggiormente ha beneficiato del rapido progresso tecnologico.
L'emocromo è ampiamente richiesto dai clinici perché è un esame necessario per la valutazione dello stato di salute del paziente; è però uno degli esami più difficili da gestire nei processi di riordino e consolidamento dei laboratori. L'emocromo è un esame multiparametrico la cui refertazione prevede l'integrazione dell'analisi automatizzata eseguita dai citometri a flusso con l'eventuale valutazione morfologica dello striscio di sangue periferico, che talvolta porta alla formulazione di un referto commentato.
Postulato che la qualità delle prestazioni, la sicurezza del paziente e un adeguato contenuto informativo del referto devono essere garantite indipendentemente dalla sede di esecuzione dell'esame. Questa può avvenire solo attraverso il governo dell'integrazione tra competenze professionali e tecnologia.
I sistemi di analisi digitalizzata dello striscio di sangue periferico possono supportare il raggiungimento di questo obbiettivo permettendo l'armonizzazione del processo di lettura dello striscio, garantendo la tracciabilità del processo, l'ottimizzazione dei tempi e facilitando la condivisione delle informazioni e delle conoscenze.
L'impiego della morfologia digitalizzata nella pratica routinaria si sta progressivamente diffondendo per gli indiscutibili vantaggi documentati, per le opportunità future di sviluppo di sistemi più performanti, di intelligenza artificiale e di incremento delle piattaforme di big-data.
Tuttavia di controparte solo una minima parte di energie sono spese per promuovere e documentare corretti percorsi di verifica e validazione di questi sistemi di analisi digitalizzata delle immagini, di verifica dell'efficienza ed efficacia diagnostica dei nuovi flussi operativi proposti e di qualificazione del personale deputato alla revisione microscopica digitalizzata.
Infatti, ad ora non è disponibile un documento che definisca limiti e regole di applicabilità della analisi morfologica digitalizzata al pari di quanto avviene per i conteggi in automazione, come pure le competenze che devono avere gli operatori che utilizzano questi sistemi, e i percorsi di verifica della qualità delle prestazioni strumentali e di verifica di qualità esterna
Sicuramente il futuro della medicina di laboratorio e dell'ematologia di laboratorio sarà condizionato e supportato da strumenti innovativi come la morfologia digitalizzata e lo sviluppo di reti neuronali, ma questa evoluzione non può prescindere dalla necessità di garantire il governo della tecnologia da specialisti di laboratorio con adeguate competenze in ambito ematologico e morfologico.

REFERENCES

- Buoro S, et al. Harmonization of laboratory hematology: a long and winding journey. Clin Chem Lab Med 2018;56:1575-8.
- Buoro S, et al. Harmonization of interpretative comments in laboratory hematology reporting: there commendations of the Working Group on Diagnostic Hematology of the Italian Society of Clinical Chemistry and Clinical Molecular Biology (WGDH-SIBioC). Clin Chem Lab Med 2018;57:66-77.
- Da Costa L. Digital image analysis of blood cells. Clin Lab Med 2015;35:105-22.
- Da Rin G et al. Multicentric evaluation of analytical performances digital morphology with respect to the reference methods by manual optical microscopy.J Clin Pathol. 2020 doi: 10.1136/jclinpath-2020-206857. Online ahead of print.
- Kratz A, et al. Digital morphology analyzers in hematology: ICSH review and recommendations. International Council for Standardization in Haematology.
- Int J Lab Hematol. doi: 10.1111/ijlh.13042. Epub 2019 May 2.

SS04-02

POCT IN HAEMATOLOGY: TECHNOLOGY AND NEW OPPORTUNITIES

R. Pajola

U.O.C. Laboratorio Analisi, ULSS 6 Euganea, Ospedali Riuniti Padova Sud "Madre Teresa di Calcutta", Monselice (Pd)

The complete blood count (CBC) is one of the most requested tests, routinely performed in the central laboratory (LAB) by large haematological analysers, useful to diagnose many diseases and manage urgent clinical decisions such as transfusion or administration of chemotherapy and antibiotics.
In recent years, rapid technological improvements led to the spread of point of care testing (POCT), performed outside the LAB and capable of providing CBC in a few minutes, measuring haemoglobin (Hb), red blood cells (RBCs), white blood cells (WBCs) with their differential count of 3 or 5 populations, platelets (PLTs) and many other parameters. Hb remains the most common POCT in haematology, essential to exclude anaemia.
There are two types of technology: small benchtop analysers and portable devices. The former are smaller and fully automated versions of LAB's analysers and, although portable, are not suitable to use at patient's bedside. The latter, some of which use disposable cartridges, do not require start-up procedures, maintenance and calibrations.
The latest generation of portable devices combines advanced digital technology with innovative technologies of viscoelastic focusing and microfluidics and techniques, such as digital microscopy and computer vision, using near infrared spectroscopy and the absorption of light at multiple wavelengths, obtaining CBC results unthinkable until a few years ago.
POCTs' accuracy is influenced by several factors: sample collection, blood type (venous or capillary) and timing. Poor finger prick technique can provide misleading results, it was proved that capillary samples significantly underestimate PLTs overestimating Hb and WBCs, but differences have not clinical relevance when the samples are collected according to standardized procedures.
POCT devices can not differentiate normal cells from pathological ones (e.g., erythroblasts, blasts, etc.). The presence of large platelets can lead to inaccurate PLT counts compared to the impedance method used in LABs. As recommended by the guidelines, due to the inherent risk of preanalytical errors and the standard risk of error during analytical and postanalytical phases, threshold values must be established to repeat CBC in a LAB.
Another consideration is POCTs' cost, which is cumulatively higher than that of a LAB-performed CBC.
Literature suggests that POCTs are not yet the ideal tools to perform CBC for diagnostic purposes, but they are useful in urgent situations such as rapid monitoring of some parameters (e.g., WBCs and Hb). Further studies are needed to confirm the promising results of POCTs and evaluate their performance even at low ranges and in pathological conditions.

REFERENCES

1. Rampoldi E., Patrucco G., Casali M., Morelli B. Carraro P. per il GdS POCT. Principi per l'implementazione e la gestione del point-of-care-testing (POCT): indicazioni essenziali. Biochim Clin 2021; 45: 312-326.
2. Briggs C., Kimber S., Green L. Where are we at with point-of-care testing in haematology?. BJH 2012; 158: 679-690.
3. Mooney C., Byrne M., Kapuya P. et al. Point of care testing in general haematology. BJH 2019; 187: 296-306.

SS04-03

DIAGNOSTICA EMATOLOGICA DECENTRATA: INGEGNERIZZAZIONE E VALUTAZIONE DEL PROCESSO

A. Brioschi

InGeSan (Ingegneri Gestionali in Sanità)
UOC Controllo di Gestione
ASST della Brianza

In un contesto in cui la Medicina di Laboratorio, fondamentale supporto nelle decisioni cliniche, è stata oggetto negli ultimi decenni di sistematiche politiche di contenimento dei costi, la valutazione del ruolo del POCT non può limitarsi ad una semplice valutazione costi/ricavi (che porterebbe a scelte di non utilizzo di tali tecnologie) ma necessita di un sistema di valutazione HTA multi-variabile, sia in fase di valutazione della scelta di implementazione della tecnologia che in fase di valutazione nel corso della vita utile del POCT.
Il Lean Management può fornire approccio e strumenti utili a "giustificare" il costo, in genere superiore a quello dell'analisi di laboratorio, con un outcome atteso migliore o ad un uso più efficiente delle risorse durante l'assistenza riducendo l'utilizzo inappropriato e gli effetti negativi del rischio legato alle attività effettuate da operatori non di laboratorio.

MEDICINA DI LABORATORIO: destinatario “privilegiato” delle azioni di contenimento dei costi

L’affermazione che “il 70-80% delle decisioni cliniche richiedono informazioni di Medicina di Laboratorio” benchè non supportata da valutazioni numeriche sistematiche, è (se non nella %) almeno empiricamente evidente nella clinica quotidiana.

Benchè i costi di laboratorio rappresentino una piccola quota della spesa totale della Sanità, la Medicina di Laboratorio è stata, negli ultimi 10/15 anni, oggetto di sistematiche politiche di riduzione dei costi (forse guidato anche dal fatto che, rispetto ad altre attività di diagnosi e cura, i costi delle attività di laboratorio sono facilmente tracciabili e monitorabili), che si sono sviluppate secondo modalità di approccio progressive:

- un primo approccio di contenimento della spesa definita attraverso “tagli lineari”;
- un secondo approccio finalizzato alla riduzione degli esami non necessari;
- un terzo approccio ha posto il focus sul controllo sistematico delle richieste “ex ante”, in particolare per i test ad alto costo, investito i dirigenti di laboratorio del compito di “cerbero”;
- il quarto approccio prevede la definizione di algoritmi di utilizzo, simili a quelli che vengono definiti nella pratica di prescrizione dei farmaci.

In tale contesto e forse nonostante o favoriti da tali politiche di taglio dei costi si è assistito all’evoluzione del sistema dei laboratori caratterizzato da un doppio fenomeno:

- riorganizzazione con consolidamento e decentralizzazione delle attività di processazione;
- sviluppo di una rete capillare di attività di prelievo distribuita sul territorio; facendo della Medicina di Laboratorio un precursore del processo di spostamento dei servizi da ospedale a territorio cui si sta assistendo in questi ultimi anni, grazie anche alla caratteristica, propria della Medicina di Laboratori e di poche altre specialità, di poter distinguere il momento di “contatto con il paziente” dal momento di effettiva erogazione della prestazione prima dell’avvento delle tecnologie a supporto della Telemedicina.

TELEMEDICINA in laboratorio

“Per Telemedicina si intende una modalità di erogazione di servizi di assistenza sanitaria, tramite il ricorso a tecnologie innovative, in particolare alle Information and Communication Technologies (ICT), in situazioni in cui il professionista della salute e il paziente (o due professionisti) non si trovano nella stessa località”
(definizione del Ministero della Salute)

Pur essendo oggetto di sviluppo già da un ventennio con l’iniziale utilizzo di POCT nelle attività di gestione dell’emergenza/urgenza ospedaliera, nell’analisi delle linee guida ministeriali del 2008 sulla telemedicina, per la Medicina di Laboratorio viene riportato un unica valutazione:

“Riorganizzazione della diagnostica di laboratorio e diagnostica per immagini

Il rilevante impatto economico ed organizzativo delle iniziative di sviluppo del settore della diagnostica di laboratorio (incluse le tecniche diagnostiche avanzate) e della diagnostica per immagini ha reso indispensabile attivare iniziative finalizzate, tra l’altro, ad assicurare l’interoperabilità dei sistemi ospedalieri e delle ASL (intra e inter-regionali), con particolare riferimento al Teleconsulto (second opinion)”

POCT: come valutare le reali opportunità per la Medicina di Laboratorio

“Per POCT si intende l’analisi eseguita vicino o al punto di cura del paziente, con il presupposto che il risultato sia disponibile immediatamente o in un lasso di tempo molto breve al fine di permettere ai clinici una diagnosi immediata e/o un’immediata decisione terapeutica”
(definizione da “Raccomandazioni per l'implementazione e la gestione del “point-of-care testing” (POCT)”)

Il costo per esame del POCT generalmente eccede quello del laboratorio clinico, di contro la remunerazione della prestazione, (ove prevista e applicabile anche alle prestazioni POCT), è pari al valore riconosciuto per l’attività effettuata in laboratorio, a fronte di un aumento del livello di rischiosità legato alla esecuzione da parte di personale non appartenente o comunque professionalmente non formato nei settori del laboratorio clinico.

In un’ottica di mera valutazione costi/ricavi il POCT risulterebbe essere una soluzione organizzativa cui preferire una gestione di “movimentazione fisica” del campione biologico, sulla quale sono stati fatti anni di efficientamento per la gestione della logistica.

La valutazione non può prescindere da altre dimensioni di analisi rispetto a quelle di costo/ricavo, considerando il POCT come modalità integrativa e non sostitutiva, da attivare quando le attività del laboratorio centrale non sono accessibili o non risultano tempestive in rapporto alla condizione clinica.

I maggiori costi devono essere “giustificati” bilanciati da un outcome atteso migliore (legato alla tempestività della cura) o ad un uso più efficiente delle risorse durante l’assistenza, (come il il contenimento delle giornate di degenza e un uso più mirato di farmaci) mettendo in atto tutte le possibili attività volte a ridurre l’utilizzo inappropriato che comporta un non giustificato incremento della spesa sanitaria nonché a ridurre gli effetti negativi del rischio legato alle attività effettuate da operatori non di laboratorio.

La valutazione HTA diviene quindi un imprescindibile strumento di programmazione nell’ambito iniziale di valutazione dell’acquisizione della tecnologia, ma deve proseguire durante tutta la vista utile del POCT con la finalità governo clinico, finalizzato a perseguire il miglioramento continuo della qualità delle prestazioni sanitarie rese, ricercando in particolare la riduzione del ricorso al POCT inappropriato ed il monitoraggio, valutazione e riduzione sistematica dei rischi.

HTA DURANTE LA VISTA UTILE DEL POCT: approccio Lean Management

L’organizzazione LEAN della produzione deve tendere in modo continuo

- ad AUMENTARE il VALORE erogato al CLIENTE tramite la riduzione sistematica degli SPRECHI
- all’ANALISI dei PROCESSI per l’eliminazione degli SPRECHI e la valorizzazione delle PERSONE

Si passa quindi da un approccio “storico” in cui il miglioramento della performance è basato sulla razionalizzazione degli «input» (risorse umane, tecnologie) ed il controllo degli «output» (volumi di produzione, tempi di attesa) arrivando alle prime analisi di «outcome» (mortalità) senza un preciso focus su come gli input siano combinati per ottenere output/outcame, ad un approccio di “miglioramento continuo” in cui l’analisi del processo di erogazione dei servizi è finalizzato ridurre ciò che non aggiunge valore per il paziente (gli sprechi),

ridurre la variabilitá evitabile ed il sovraccarico (entrambi fonti di errore).
Nella valutazione del processo di utilizzo del POCT devono essere, attraverso la valutazione del processo in ogni singola azione e nelle modalità in cui le azioni si combinano e si sequenziano, individuate e ridotte tutte le fonti di "spreco"

- sovrapproduzione: produrre più del necessario per avere a disposizione ciò che è utile
- attese: i tempi morti che si generano tra le diverse fasi del processo quanto non si susseguono in modo sincronizzato
- trasporti: spostamenti dei pazienti/clienti o dei materiali quanto non siano necessari, evitabili, senza valore aggiunto per il processo
- operazioni inutili: errato utilizzo delle risorse durante le attività che in genere si associano a ridondanza di operazioni, senza valore aggiunto
- scorte: surplus di materiali immagazzinati che aspettano di essere utilizzate, con conseguente costi di gestione, obsolescenza, inutilizzo
- movimenti: spostamenti inutili degli operatori per attività non a valore aggiunti (reperimento materiale, postazione di lavoro in altra sede)
- difetti: di prodotti o di servizi che danno luogo a un risultato «non conforme» e ad un conseguente ritardo nelle attività di processo e ad una riprocessazione
- competenze: professionalità poco valorizzate, carichi di lavoro non valutati in base ai profili e alla capacità, formazione carente

Puntare alla "perfezione" è l'obiettivo del Lean Thinking, intesa come MIGLIORAMENTO CONTINUO. L'approccio in contrapposizione al concetto di innovazione radicale tipico «occidentale» è quello di cercare un miglioramento moderato ma continuo: individuare uno spreco, attivarsi per ridurlo ed eliminarlo, consolidare il risultato e… non accontentarsi! individuare un altro spreco, attivarsi per ridurlo ed eliminarlo, consolidare il risultato e… individuare uno spreco, attivarsi per ridurlo ed eliminarlo……
In tal senso strumenti propri della LEAN quali

- l'utilizzo dei sistemi di "analisi delle cause radice" finalizzate ad individuare le vere cause dei problemi e individuarne conseguentemente la soluzione, senza arrivare alla soluzione (in genere errata o incompleta) prima di aver individuato l'effettivo problema;
- la definizione di indicatori di processo per misurare il sistema "AS IS" e definire il sistema "TO BE" per guidare ogni azione di miglioramento, necessari a definire il raggiungimento di un obiettivo;
- l'esplicitazione della necessità di una fase di "mantenimento" dei risultati raggiunti attraverso azioni programmate ed esplicite di monitoraggio, verifica ed audit, formazione e informazione, senza la quale in genere la qualità della prestazione tende a ridursi;

possono fornire gli strumenti su cui definire il percorso di ricerca/mantenimento/miglioramento della performance di un POCT.
Il lean thinking non punta alle soluzioni "preconfezionate", ma a far sì che siano le persone a sviluppare le soluzioni; questo per un POCT, un sistema "lontano" dal laboratorio, è coerente con la necessità di coinvolgimento attivo del personale esterno al laboratorio nella ricerca del miglioramento in ottica di riduzione del ricorso inappropriato e della minimizzazione degli errori.
In tal senso ben si coniuga con l'approccio Lean quanto previsto dalle "Indicazioni essenziali" SIBIOC in termini di attori da coinvolgere e fasi di processo da valutare.
Le indicazioni infatti prevedono la costituzione di un comitato multidisciplinare, finalizzato a facilitare la progettazione e la pianificazione di tutte le attività, facendo emergere le necessità dei vari gruppi e raccogliendo proposte, indicazioni correttive e possibili soluzioni.
In tale comitato trovano il proprio ruolo tutti gli attori principali di un progetto Lean:

- Direttore Sanitario – sponsor del progetto e facilitatore nei momenti critici;
- Responsabili delle diverse fasi del processo (direttore del laboratorio, direttore di farmacia, responsabile servizio di ingegneria clinica, responsabile dei sistemi informativi, referente di UO)
- Personale effettivamente coinvolto nelle fasi di processo (coordinatore POCT con funzioni di POCT Manager di laboratorio, tecnico di laboratorio, consulente infermiere; ecc.)

Nello stesso documento vengono identificate alcune delle fasi del processo di implementazione delle attività di un POCT (controllo del processo, manutenzione della strumentazione, controllo elettronico, controllo di qualità esterno, compatibilità dei risultati, analisi degli indicatori di qualità, ecc) e le attività di sviluppo e mantenimento delle competenze del personale (verifica dei fabbisogni formativi, formazione, re-trainig).

REFERENCES

- "Lo spirito Toyota. Il modello giapponese della qualità totale. E il suo prezzo" 1988 – Taiichi Onho
- "La logica diagnostica di laboratorio ed il Point of care testing" 2001 - Paolo Rizzotti - Riv Med Lab - JLM
- "Raccomandazioni per l'implementazione e la gestione del "point-of-care testing" (POCT)" 2011 - Francesca Di Serio, Tommaso Trenti, Paolo Carraro – SIBioC Documents "TELEMEDICINA Linee di indirizzo nazionali" 2012 - Ministero della Salute
- "Contenimento dei costi nel laboratorio clinico: razionamento o razionalizzazione?" 2015 - Mario Plebani – SIBIOC Documents
- "Principi per l'implementazione e la gestione del point-of-care-testing (POCT): indicazioni essenziali" 2021 - Erica Rampoldi, Giovanna Patrucco, Marco Casati, Benedetto Morelli, Paolo Carraro – SIBioC Documents

SS04-CO03

HEMATOLOGICAL DIAGNOSTICS: THE TELEMEDICINE PROJECT FOR THE LABORATORY SPREAD ACROSS A LARGE TERRITORY

M. Lorubbio[1], F. Baldelli[1], E. Bromo[5], G.P. Caldarelli[4], C. Donnini[1], S. Fabbroni[1], A. Fanelli[1], M. Fantacci[2], L. Gasbarri[1], M. Mazzi[4], A. Periccioli[3], P. Pugliano[4], C. Rapini[2], A. Rebuffat[3], A. Sereni[1], M. Sorini[1], E. Tripodo[1], A. Ognibene[1]

[1]Clinical Chemical Analysis Laboratory, San Donato Arezzo Hospital
[2]Clinical Chemical Analysis Laboratory, Montepulciano Valdichiana Reunited Hospital
[3]Clinical Chemical Analysis Laboratory, Hospital Alta

Valdelsa
[4]Clinical Chemical Analysis Laboratory, Misericordia Grosseto Hospital
[5]Dip. del Farmaco, Misericordia Grosseto Hospital

Introduction The territory of the USL TUSCANY SOUTH EAST (TSE) has an area of 11,557 sq km with 850,446 inhabitants. The use of information and communication technologies (ICT) and E-Health can contribute to a reorganization by moving the focus of health care from the hospital to the territory. The aim of the present project is to evaluate of the complete blood count (CBC) test and the peripheral blood smear through digital images, shared and available to the team of the 12 TSE laboratories. During implementation, the image analyzers and the staining adopted were compared, together with the quality indicators (QI) to support the new flows implemented between the peripheral laboratories and the Hub laboratory. Materials and methods The connection network between all TSE Laboratories was guaranteed by the DMS (DASIT Management System) WEB application, for XN (Sysmex) instruments and, Caresphere TMXQC for the management of CQI. The cellular digital images were shared through digital online archives, managed using the DI60 and and DC-1 (CellaVision™). 135 peripheral blood smears were performed using SP10 (HUB) and HemaPrep (Spoke), staining May-Grünwald Giemsa (Sysmex) and Romanowsky-type (RAL Diagnostics), respectively. For study QI, 26 CBC performed in the peripheral laboratories were reanalyzed after 4-6 h at the Arezzo Laboratory. Statistical analysis was performed using SPSS and GraphPad Prism. Results The Passing-Bablok and Bland-Altman plot analysis performed for comparison of all elements of the blood count test, provided excellent results between the technologies and the different cell staining used (data not shown). The MCV and PLT parameters of the CBC, performed in the spoke laboratories and reperformed in the Hub laboratory after 4-7 hours, showed a statistical significative differences of 3.18(±0.66) fL and 10.69 (±17.83) 103µL respectively. Conclusions The organization proposed in the project improves the analytical quality, harmonises the reporting and interpretation of analytical data, promotes uniform training, preparing for continuous professional comparison.This approach represents a model that contrasts with centralization, favoring the concept of widespread laboratory medicine, while maintaining an advantageous cost/benefit ratio.

SS04-CO04

LEUCOCYTE DIFFERENTIAL AND MORPHOMETRIC PARAMETERS WITH MINDRAY BC-6800 PLUS: A POSSIBLE PREDICTIVE TOOL TO DIAGNOSE SEPSIS AND SARS-COV-2 INFECTIONS.

M. Pelagalli[1,2], A. Giovannelli[1,2], C. Calabrese[1,2], S. Sarubbi[1,2], M. Minieri[1,2], M. Nuccetelli[1,2], M. Pieri[1,2], S. Bernardini[1,2]

[1]Department of Laboratory Medicine, "Tor Vergata" University Hospital,Rome, Italy
[2]Department of Experimental Medicine, University of "Tor Vergata",Rome, Italy

Background: Sepsis is an infectious disease (the etiology can be viral or bacterial) with hight mortality, threatening human health. Clinicians need to diagnose the patient's infection in time and look for pathogens in order to develop an effective treatment plan; therefore, a quickly and early screen to diagnose sepsis has become an urgent problem in clinical laboratories. Different inflammatory factors are used to diagnose the sepsis; CRP, IL-6, PCT, ADM, lactate, D-dimer etc., but they also have limitations such as insufficient sensitivity and specificity and requiring additional examination cost. The aim of this study is to use leucocyte counts (neutrophils and monocytes that are activated from pathogenic virus or bacteria) and others morphological change with Mindray BC-6800-plus platform to diagnose sepsis early, quickly, conveniently and at low cost.
Methods: A total 957 EDTA-k2 anticoagulant venous whole blood samples were collected: 70 control patients (blood donors) with a normal complete count blood and negative VES, and 887 samples hospitalized at the emergency department with symptoms attributable to sepsis with PCT request. All data was divided in 4 groups: control group, group where sepsis cannot be confirmed, group with confirmed sepsis diagnosis and a group with sepsis from SARS-CoV-2 infection. Morphometric and numeric parameters are reported with Mindray BC-6800 plus: blood count like positional parameters X, Y, Z of neutrophils, lymphocites and monocytes, PLT, NLR (neutrophil lymphocyte ratio) and IMG (index of immature granulocytes). For statistical analysis was used Shapiro Wilk test for distribution analysis and the non parametric Kruskal Wallis test to evaluate significative differences among the groups ($p < 0.05$) and also examined ROC curve analysis.
Results: There is a statistically significant difference between control group and sepsis group for haematological parameters: positional parameters (Neu X, Y, Z; Mon X, Y, Z and Lym X, Y, Z), IMG, NLR, PLT. The roc curves highlight acceptable sensitivity and specificity values for some haematological parameters and suggest a possible cut-off. Conclusions: The BC-6800 plus can help the diagnosis of sepsis upon the admission to the emergency department using some morphological positional parameters.

SS05 - Cure primarie, poct e prove di efficacia: la sinergia necessaria

SS05-01

EBLM: ITS VALUE AND ROLE IN DECENTRALIZED DIAGNOSTIC AND PROXIMITY MEDICINE"

V. Pecoraro

Dipartimento integrato di Medicina di Laboratorio e Anatomia Patologica, Modena

Evidence based laboratory medicine (EBLM) focuses on the use of diagnostic tests to improve patient outcomes. Principles of EBLM, integrating the best research and the clinical expertise, could be applied also for point of care testing (POCT) (1). POC are tests conducted near the site of patient care, outside of the laboratory, usually performed by patients or clinical personnel not trained in laboratory medicine. POCT require smal sample volumes, minimize pre-analytical errors, and reduce

alterations of labile analytes. However, when used appropriately, could improve the patients outcomes by providing faster results and earlier therapeutic strategies (2). Instead, its over or incorrected use could leads a patient risk and potential increase of healthcare costs. We assessed, throught a systematic review of the recent scientific letterature, the accuracy of the POCT on troponin, procalcitonin, C-reactive protein, parathyroid hormone, INR and d-dimer, and evaluate the impact of faster results on patient management. Studies measuring PCT, PTH and d-dimer reported a limited impact on diagnostic decisions. Instead, studies on CRP claimed a significant reduction of antibiotic prescription. Several authors evaluated troponin and INR reporting faster decision-making without any improvement in clinical outcome. Faster results are often translated in better outcomes, without evidence to support this conclusion. So, it is important that the POCT practice is evidence-based looking for evidence of whether POCT confers any advantage in clinical decision making in different scenarios. In some settings, such as rural enviroment, a rapid availability of cardiac troponins or other analytes can help clinicians to rule out or rule in disease, without tranfer patient in other center, avoiding unnecessary costs (3). Likewise, in Emergency Department, availability of more rapid results with POCT help clinicians to refere patients, but does not always translate into shorter stays (4). The satisfactory analytical performance, together with an excellent practicability, suggest that the POCT represents an important technologycal advance in patient care, but, the lack of evidence about the patients outcome invite healthcare workers to use it with judgement.

REFERENCES

1. Price CP. Point of care testing. BMJ 2001; 322: 1285–1288.
2. Pecoraro V, Banfi G, Germagnoli L, Trenti T. A systematic evaluation of immunoassay point-of-care testing to define impact on patients' outcomes. Ann Clin Biochem. 2017 Jul;54(4):420-431.
3. Herd GCE, Musaad SMA. Point-of-Care Testing in Rural and Remote Settings to Improve Access and Improve Outcomes: A Snapshot of the New Zealand Experience. Arch Pathol Lab Med. 2021 Mar 1;145(3):327-335.
4. Alter DN. Point-of-Care Testing for the Emergency Department Patient: Quantity and Quality of the Available Evidence. Arch Pathol Lab Med. 2021 Mar 1;145(3):308-319.

SS05-02

EBLM AND BLOOD GAS ANALYSIS PARAMETERS: WHICH IS MANDATORY TO MEASURE.

E. Rampoldi

Coordinatrice del Gruppo di studio POCT per SIBioC

Arterial and venous blood gas analysis reveals oxygenation and acid-base status of the body. The analysis usually includes: pH, PaO2, PaCO2 and a wide range of different analytes, besides other several derivated (calculated) parameters, as HCO3-, BE, anion gap.

Arterial pO2 (PaO2) is the most important variable to assess the oxygenation status and can't be substituted by venous blood or capillary measures of O2 (1).

American Association for Respiratory Care (AARC) updated Recommendations on blood gas analysis (BGA) and hemoximetry (2). The clinical practice guideline is based on 237 clinical trials, 54 reviews, and 23 meta-analyses searched in MEDLINE, CINAHL, and Cochrane Library database. Hemoximetry is recommended to determine the impact of dyshemoglobins on oxygenation. Some calculated values may be in error, e.g. calculated SaO2 may overestimate oxyhemoglobin saturation in the presence of carboxyhemoglobin or methemoglobin. Moreover, the presence of high concentration of fetal hemoglobin may also be a problem if blood gas analyzer does not detect it, as instrument assumes hemoglobin to be of the adult type, and therefore the calculated blood gas oxygen saturation values are underestimated.

In critically ill patients many other analytes have been used to estimate the severity of disease and try to prognosticate morbidity and mortality. No measurements can encompass the complexity of a disorder, but lactic acid can approach that goal (3) Indeed lactic acidosis is the most frequent metabolic acidosis and many causes are reported for lactate increase, not only hypoxia: the higher the lactate concentration, the worse the outcome. The initial values have a prognostic significance, but serial measurements are more valuable for prognosis. Conductivity-based Hematocrit (Ht) estimations have limitations. Abnormal protein concentration will change plasma conductivity. Low protein concentration, resulting from dilution of blood with protein-free electrolyte solution during surgery, will result in erroneously low Ht value. Conductivity-measured hematocrit during and after surgery could produce inaccurate results when Ht are lower than 30%, and, therefore, result in unnecessary red cell transfusions in some patients. In any situation, to correctly interpret BGA results history should be always considered: reasons for presentation, information concerning events, environment, trauma, medications, poisons, toxins and an accurate physical examination should be carefully collected.

REFERENCES

1. Acute respiratory distress syndrone: the berlin definition, Ranieri MV et al 2012 Jun 20; 307(23):2526-33.doi: 10.1001/jama.2012.5669.
2. AARC Clinical Practice Guideline: Blood Gas Analysis and Hemoximetry: 2013 Michael D Davis, Brian K Walsh, Steve E Sittig, and Ruben D Restrepo Respir Care 2013; 58(10):1694 –1703.
3. N Engl J Med Lactic Acidosis 2014; 371:2309-19. DOI: 10.1056/NEJMra1309483.
4. Conductivity-based Hematocrit measurement during cardiopulmonary bypass. Steinfelder-Visccher J et al. 2007; J Monitoring and Computing, 27:7-12.

SS06 - Big data e valutazione dei risultati prodotti dalla diagnostica di laboratorio nei percorsi di cura dei pazienti territoriali

SS06-01

INTELLIGENZA AUMENTATA E IL VALORE DELL'INNOVAZIONE: I MODELLI CHE SPIEGANO E PREDICONO

N. Musacchio

Gli algoritmi di apprendimento automatico, o machine learning, si sono dimostrati molto efficaci nel prevedere il comportamento dei fenomeni rappresentati nei dati biomedici.
Gli algoritmi di machine learning più comunemente utilizzati, come ad esempio le reti neurali artificiali, producono risultati cosiddetti a "scatola nera", ovvero:

- un insieme complesso di equazioni matematiche che non possono essere interpretate da persone che non abbiano specifiche competenze di tipo matematico;
- modelli predittivi che non forniscono nessuna spiegazione sulla motivazione sottostante alla previsione stessa.

Quando si applica il machine learning a dati come le immagini, gli algoritmi black box non sono un problema, poiché il valore del modello risiede nella sua accuratezza nel rilevare la presenza di determinati pattern, riconducibili, per esempio, alla presenza di un tumore. Tuttavia, se lo scopo è comprendere in maniera più approfondita uno specifico fenomeno, è fondamentale capire, per esempio, perché il modello predittivo ha classificato un particolare paziente come 'a rischio' o 'non a rischio', elicitando le caratteristiche associate a questa classificazione.
Una specifica tecnica di ML, il “metodo a generazione di regole” di Rulex, costruisce modelli basati su regole intelligibili che consentono di ricavare importanti conoscenze sulle variabili incluse nell'analisi e sulle loro relazioni rispetto agli esiti del fenomeno analizzato.
L'intelligenza artificiale "Clear box" apre a entusiasmanti scenari d’implementazione di una vera e propria intelligenza aumentata, in cui uomini e macchine creeranno una sinergia - controllata dall'esperto – che potrà concretamente migliorare la qualità delle cure.
Ultimo, ma non meno importante, secondo il GDPR i dati personali devono essere trattati in modo trasparente e qualsiasi cittadino europeo ha il diritto alla spiegazione qualora una decisione che lo riguardi si sia basata su algoritmi di machine learning: la AI 'clear box' permette di operare nel pieno rispetto della legislazione europea.

SS06-02

THE RISE OF THE UBIQUITOUS LAB

G. Giannella

Healthcare is the one of the largest success stories of our times. Technology is another of the largest success stories of our times. People expectations about healthcare+technology is at its absolute peak. We are in the middle of a health-tech secular change. This is for good. This is unstoppable. This is the best part of the story. Yet, healthcare spending is unsustainable in an aging world. Technology, as every tool, brings its risks. Global levels of assistance are outrageously unequal. Mental disorders are exponentially growing. That’s the other part of the story. How will the lab of the future adapt to the entire story? Will it “just” be able to sustain the health-tech revolution, or will it also play a role in making global health systems more sustainable, equal, and safer?
The speaker of this panel will present his view on how “deeptech” (a synergetic combination of leading-edge technology which today assembles Internet of Things, Artificial Intelligence, Digital and Space) coupled with rising individual expectations for highly personalized and accessible healthcare, will redefine the boundaries of healthcare system and the concept itself of lab.
Internet of Things will be the main key to acquire all the right data. Trillions of “sensors” supporting data gathering from multiple sources: humans, plants, things, places, food, animals, environment. Contextualized data gathering to acquire different data in different contexts, “actuators” instructing devices to do the right thing in the right moment, surveillance networks for enhanced threats.
Artificial Intelligence will be non-optional. With health-related knowledge doubling in months, AI will become a mandatory survival kit. Yet, it still will see things that human eye might miss. Or making correlations that are simply too difficult anyway else. Yes, it will be both defensive for professionals and offensive to diseases, if used in the right way, as every tool.
Digital will influence behaviors, create communities, and redefine the patient-professional interaction. With big part of the clinical outcome depending on context and behaviors, Digital will help to “nudge” patients with personal, doable, life-enhancing tips. But Digital is also the “home of increased expectations”. Patients are individuals, parents, children, workers, citizens, consumers, with ever-growing expectations on what and how can be done through a smartphone. Health won’t make any exceptions.
Space and satellite technology will provide the communication background for all above, from remote surgery to distributed expert network, etc. But Space will also bring additional data coming from macroscopic data gathering, earth observation, context-related data and gravity-less phenomenon analysis.
Can the lab of the future stay immune from all above? Hard to believe. While exact predictions are useless, some trends are clearly visible and point to the raise of a next-generation ubiquitous lab. An “always-on” set of competences, data, technologies, uniquely positioned to close the fracture existing between everyday life/health of individuals and the infinitely smaller portion of its current clinical representation.

SS06-CO05

LARGE GENOMIC ALTERATIONS (LGAS) PROFILES IN HBOC PATIENTS USING SHALLOW WGS (SWGS) PIPELINE FOR THE ASSESSMENT OF HOMOLOGOUS RECOMBINATION DEFICIENCY (HRD) SCORE

G.L. Scaglione, C. Nardelli, M. Setaro, E.D. Capoluongo

Lab. Genomica Oncologica, CEINGE Biotecnologie Avanzate S.C.R.L., Napoli

Background: The homologous recombination (HR) pathway is essential for DNA double strand break (DSB)

repair and involves several genes. HR deficiency (HRD) arises upon inactivation of BRCA1/2, RAD51C or PALB2. The impairment of this pathway is a common characteristic of many tumors and it is frequently observed in breast and ovarian cancer. Consequently, accurate detection of HRD is of clinical relevance as it is indicative of sensitivity to targeted therapy with poly ADPribose polymerase inhibitors (PARPi) as well as to DNA damaging reagents.
Methods: Shallow Whole Genome Sequencing (sWGS) was performed on sixteen ovarian cancer (OC) samples. The training set included 13 samples (6 somatic, 7 germline) carrying both BRCA+ve (n=9) and BRCA-ve (n=4) status. The germline and somatic samples were prepared according to SeqCap EZ HyperCap protocol (Roche). Briefly, 50 ng of input DNA was used for libraries preparation using the KAPA HyperPlus Library Preparation Kit (Roche). Samples were then pooled and sequenced on NextSeq550 Dx platform (Illumina). Sequencing files were quality checked, analyzed and processed using our dedicated bioinformatics pipeline. In this workflow, LGAs profiles were calculated using whole genome sequencing data at low coverage (0.4-1.0X) using different sliding window size spanning 5 to 1000 Kbases. The HRD score was then estimated by measuring the level of agreement in the segmentation profiles of each samples.
Results: The BRCA status was assessed in 13 samples (training set) and the HRD score was estimated as follow: 2 of the 3 somatic BRCA positive (sBRCA+ve) samples were classified as HRD positive while 2 out of 3 sBRCAve samples were scored as negative. As expected, both positive (+ve) and negative (-ve) germline BRCA (gBRCA) samples were classified as HRD negative. Lastly, Among the remaining samples (n=3) for which the germline status of BRCA genes was not available, the algorithm classified 1 sample carrying PALB2 CNV as HRD positive.
Conclusions: Germline BRCA1/2 mutation status is currently the main genetic biomarker of HRD but it has its drawbacks: among others HRD can be driven purely by somatic events. In this scenario we have customized a simple and robust bioinformatics workflow to infer the HR status of breast and ovarian tumor based on sWGS to support patients' treatments and follow up strategies.

SS06-CO06

THE BIG DATA ANALYSIS APPLICATION TO EVALUATE THE CLINICAL UTILITY OF IGM ANTI SARS-COV-2 DETERMINATION: THE EXPERIENCE OF MODENA

V. Pecoraro[1], T. Pirotti[1], T. Trenti[1], M. Plebani[2]

[1]Department of Laboratory Medicine and Pathology, Azienda USL of Modena, Italy
[2]Department of Laboratory Medicine, University-Hospital of Padova, Italy

Background: Serological tests identifying SARS-CoV-2 IgG and IgM in serum play an important role in understanding the disease epidemiology. However, their immunological significance are currently undefined. There are many methods available for the detection of specific Abs whit suboptimal diagnostic accuracy and relatively high throughput capacity and less stringent specimen requirements compared to RNA-based assays. We aimed to assess the clinical utility of IgM detection in SARSCoV- 2 using the big data analysis. Methods: We conduct a retrospective study analyzing with a big data analysis all samples collected between 11 March and 30 September 2020. All serum samples received at the laboratory were processed using qualitative and commercially available rapid lateral flow immunoassay tests for 2019-nCoV IgG and IgM. Positive results were confirmed using a chemiluminescent method. Subjects with a positive result were contacted from the Department of Public Health for further tests (viral RNA research or subsequent serological tests) for definitive diagnosis.Results: A total of 69,343 serological tests (in 42,911 subjects) and 140,065 oropharyngeal or nasopharyngeal swabs (in 88,771 subjects) were performed. 94.5% of subjects screened (n=40,559) had negative results for both IgG and IgM. Of the 640 subjects with both IgG and IgM positive results, viral RNA research confirmed positivity in 16%. Of the subjects with IgG negative and IgM positive results, a positivity was confirmed in 1.4% (n=7/478) subjects. Subsequent serological testing confirmed IgG positivity in 8 subjects (1.6%). Conversely, in subjects with IgG positive and IgM negative results, a positivity was confirmed in 7.9%. Therefore, analysis suggests that up to 94% of serological test results of IgM positivity and IgG negativity are false positive whereas, serological test results of IgG positive and IgM negative are confirmed true positives in around 7.9% of subjects. Discussion: Our study, based on big data analysis application, confirms the scarce clinical utility of IgM anti SARS-CoV-2 detection in COVID-19 management, and underlines the responsibility of laboratory medicine professionals to highlight limitations of the SARS-CoV-2 serological tests due to uncertainty in their interpretation.

SS07 - La diagnostica molecolare decentrata: "rischi e opportunità"

SS07-01

IL RUOLO DEI PRESCRITTORI: IL PDTA NEI TUMORI OVARICI

P. Scollo

Dipartimento Materno Infantile e dell'U.O.C. di Ginecologia ed Ostetricia
Azienda Ospedaliera per l'Emergenza Cannizzaro (A.O.E.C.) di Catania.

Il carcinoma ovarico rappresenta la settima neoplasia più frequente nella popolazione femminile mondiale e la principale causa di morte tra i tumori ginecologici. In Italia, sono stati registrati circa 5300 nuovi casi nel 2019, ed è la quinta causa di morte per cancro nelle donne di età compresa tra 50 e 69 anni, con una sopravvivenza netta a 5 anni dalla diagnosi stimata intorno al 40%.
Ad oggi mancano delle strategie di screening efficaci per l'identificazione precoce della malattia, e l'assenza di sintomi predittivi ed il ritardo nella diagnosi che ne consegue fa si che oltre il 75% delle donne al momento della diagnosi presenti un tumore in stadio avanzato necessitando di una gestione multidisciplinare da parte di professionisti con specifiche competenze. Solo centri di riferimento possono offrire un'assistenza così complessa

ed è ormai documentato come le curve di sopravvivenza delle pazienti migliorino (> 40%) in centri con esperienza specifica per il trattamento del carcinoma ovarico. La disponibilità di una guida nei percorsi diagnostici è una esigenza per medici di medicina generale e specialisti di altre discipline che scaturisce dalla necessità di dover garantire al paziente il percorso diagnostico più appropriato, meno impegnativo, più utile e meno dispendioso. Lo scopo dei PDTA è quello di incrementare la qualità dell'assistenza percepita ed effettivamente erogata, migliorando gli outcomes e promuovendo la sicurezza del paziente attraverso l'utilizzo delle giuste risorse necessarie. L'approccio chirurgico riveste un ruolo fondamentale ed imprescindibile nel programma di cura ed il residuo tumorale assente è stato definito come l'unico residuo tumorale che si associ a curve di sopravvivenza ottimali e anche la chemioterapia antiblastica che segue sempre la chirurgia nel cancro ovarico avanzato, ottiene risultati migliori dopo una chirurgia ottimale. Esperienza, cultura e preparazione tecnica dell'operatore hanno un impatto sulla curva di sopravvivenza della paziente motivo per cui è fondamentale che tale procedura sia eseguita in centri di riferimento specializzati, con una esperienza del chirurgo ginecologo oncologo certificata da percorso formativo o casistica adeguata ed una organizzazione strutturale complessiva multidisciplinare, in modo da garantire la migliore sequenza terapeutica per la paziente. La prima rete di riferimento e diffusione dei PDTA è costituita dalla medicina generale. Non si può infatti prescindere dalla condivisione con tutta la rete regionale dei medici curanti che sapranno così a chi inviare la paziente con sospetto o diagnosi già accertata di cancro ovarico, per un percorso diagnostico e terapeutico adeguato anche nei tempi permettendo un feedback sulle condizioni ed i percorsi clinico-terapeutici delle singole pazienti. Inoltre vanno incentivati i rapporti informativi e di riferimento con le associazioni di volontariato e le associazioni di pazienti che costituiscono patrimonio fondamentale nella realizzazione e sviluppo di informazione, cultura sanitaria di prevenzione primaria e secondaria e di affiancamento nelle cure domiciliari o in strutture di assistenza anche ai malati terminali.

SS08 - Young Scientists - Evoluzione della Medicina di Laboratorio: strategie e nuove sfide

SS08-CO09

MELANOQ WEB-APP: AN INNOVATIVE TOOL FOR COLLECTING, HARMONIZING, AND MANAGING CLINICAL AND GENETIC DATA OF MELANOMA PATIENTS USING A WEB-BASED PLATFORM

C. Pellegrini, L. Cardelli, M. Mastrangelo, M. Bressan, M.C. Fargnoli

Dermatologia, Dipartimento di Scienze Cliniche Applicate e Biotecnologiche, Università degli Studi dell'Aquila

With more than 320,000 new cases and 57,000 deaths worldwide in 2020, melanoma remains one of most aggressive cancer globally. The incidence varies widely among white-skinned populations and has significantly increased in recent years in Australia, US and in Europe, including in the Mediterranean area. Given the heterogeneous recording of epidemiological, clinical and genetic variables across melanoma studies, the MelaNostrum Consortium was confronted with the difficult task of harmonizing all information from different international centers to perform association studies. Therefore, MelaNostrum investigators developed a questionnaire for data collection that could be used as a full or itemized template for the standardization. On the base of that questionnaire, we built a web-based tool that allow to collect data taking advantage of a telemedicine approach. The App allows to complete online the MelanoQ questionnaire using a tablet, and automatically generates the database with all the collected data of each patient. Similar to the MelanoQ questionnaire, the MelanoQ Web-App is organized in 4 main sections (A-D) and includes a total number of 64 items related to: general and demographic information (section A); phenotypic, UV exposure risk factors and lifestyle habits (section B); clinical examination, medical history and family history (section C); tumor characteristics, including histology, staging and molecular profile (section D). Different subsections are designed for self-administration, patient/ control interviews performed by a physician or study nurse, and data collection from medical records. A specific attention has been paid to the anonymization of data, to solve privacy concerns and to collect different signed consensus format by international patients.In conclusion, we sought that a web-tool to generate a comprehensive database allowing to pool data on melanoma from different centers world-wide is of great opportunity for clinicians and for patients.

SP01 - Il ruolo del POCT nella diagnosi delle sindromi coronariche acute

SP01-01

hs-cTnI: RETI POINT OF CARE E RISCHIO CLINICO

M. Mele

Giomi
Unità operativa: Laboratorio Analisi Cliniche Struttura:ICOT Città: Latina Mansione: Responsabile del Servizio Laboratorio Analisi Cliniche

La ISO 15189 e la ISO 22870 ci impongono l'adozione di cruscotti gestionali, indicatori e analisi del rischio, nell'ottica di un miglioramento continuo della qualità del dato diagnostico e riduzione del TAT. Nella gestione delle SCA-NSTEMI dobbiamo determinare il peso che, la caratteristica della Troponinal- HS (CV contenuto entro il 10%) e il valore delta del 20% come variazione significativa nel monitoraggio, potrebbero avere nell'inficiare il valore predittivo negativo di un dato rilasciato in assenza di un controllo di qualità interno che non restringa l'imprecisione analitica, soprattutto per i valori di concentrazione vicini ai limiti decisionali. Nel nostro laboratorio è stato reclutato un campione di pazienti con età > 65 anni, degenti nella struttura e sottoposti ad interventi di sintesi o protesizzazione di fratture di femore entro le 48 ore dal ricovero e aventi sintomatologia riconducibile a cardiopatia ischemica (dispnea, dolore toracico, aritmie ed ipotensione). Per tali pazienti è stato misurato il dosaggio

delle troponine su POCT sottoposti a controlli di qualità parte terza; tali controlli sono stati validati da software gestionale al fine di ridurre la variabilità analitica e consentire il monitoraggio dei pazienti a rischio, con protocollo 0-1h, direttamente nelle TIPO ad opera dei cardiologi; questo ha inoltre permesso al laboratorio di misurare, valutare e ridurre il rischio di causare danni al paziente attraverso il sistema IQCP (Individualized Quality Control Plan) e la supervisione dei sistemi integrati come da linee guida a garanzia e tutela del medico e soprattutto del paziente.

SP01-CO10

EVALUATION OF A HIGH-SENSITIVITY CARDIAC TROPONIN POINT-OF-CARE ASSAY: A COMPARISON WITH A LABORATORY PLATFORM

R. Aloe[1], P. Avanzini[1], R. Musa[1], P. Cerati[1], M. Di Pietro[2]

[1]SSD Biochimica ad Elevata Automazione, AOU Parma
[2]Laboratorio Unico Metropolitano (LUM), AUSL Bologna

Background: Until recently, high sensitivity in cardiac troponin testing was achieved exclusively by laboratory platforms, whereas point-of-care systems lacked the required analytical performance. In 2020, however, the first high sensitivity cTn POC assay (TriageTrue, Quidel) was successfully evaluated (1) and assay-specific cutoffs for the 0/1-h algorithm were included in the ESC guidelines for the management of NSTEMI (2). In this work, the performance of TriageTrue in comparison with the hs-cTn assay currently in use in our institution (Access Hs TnI, Beckman Coulter) was evaluated.
Methods: Linearity of TriageTrue was assessed on 11 plasma samples, each in 5 replicates (cTn = 3.13–800 ng/L). Precision was evaluated on 3 pools with different concentrations (5 aliquots/pool × 5 days). For the comparison study, 146 plasma T0/T1 samples coming from 73 ED patients with chest pain were tested using both methods. Agreement was assessed with Spearman's correlation, Passing-Bablok regression and Bland-Altman analysis (MedCalc 18.6).
Results. Linearity: Spearman's correlation coefficient = 1.000; p <0.001. Total precision (CV): 4.5% (low), 9.2% (medium), 9.0% (high). Within-run precision: 4.82%– 9.25%. Passing-Bablok regression: intercept = 0.6674 (95% CI: -0.6031–1.2862), slope = 0.886 (95% CI: 0.8301–0.9792) for T0; intercept = 0.01802 (95% CI: -1.0898–0.07439), slope = 0.9463 (95% CI: 0.8777–1.0347) for T1. Bland-Altman analysis: mean bias = -0.4 ng/L (T0); 1.4 ng/L (T1). Spearman's correlation: 0.914 (95% CI: 0.865–0.946; p <0.001) for T0; 0.924 (95% CI: 0.880–0.952; p <0.001) for T1.
Conclusion: CV was <10% for all the analyzed pools. Precision was particularly high (CV = 4.5%) in the low pool, which is relevant for the reduction of analytical noise and the reporting of small cTn variations around the 99th percentile URL. The tested methods show great concordance, with high correlation for T0/T1 samples and a slight proportional difference at T0. Overall, TriageTrue is a valid alternative to the tested laboratory assay and its adoption by EDs may considerably reduce turnaround times and streamline clinical decision-making at the onset of myocardial infarction.

REFERENCES

1. Boeddinghaus et al., JACC 2020, 75, 1111–1124.
2. https://doi.org/10.1093/eurheartj/ehaa575.

SP02 - Alleanza per la qualità e miglioramento degli outcome clinici

SP02-01

RISK MANAGEMENT FOR POINT-OF-CARE TESTING

J.H. Nicholas

Vanderbilt University Medical Center, Nashville, Tennessee, USA

Introduction: Point-of-care testing (POCT) is laboratory testing conducted close to the site of patient care. POCT is growing in popularity with manufacturers offering a wide menu of tests and devices where the operator can obtain a rapid test result with the potential to initiate faster patient care decisions. But POCT is not fool-proof, and any test can and will fail if operated under the wrong conditions.
Methods: Risk management is a process where laboratories can assess their weaknesses, implement a control plan to detect and prevent erroneous results, and monitor the effectiveness of their plans.
Results: The Clinical and Laboratory Standards Institute (CLSI) EP23-A: Quality Control Based on Risk Management provides guidance based on risk management for laboratories to develop quality control plans tailored to the particular combination of measuring system, laboratory setting, and clinical application of the test.
Discussion: This presentation will describe how laboratories can partner with manufacturers to conduct risk assessments and implement quality control plans in their laboratory and at the point-of-care. The advantages of utilizing a risk management approach to controlling laboratory errors will be emphasized along with the efficiencies gained from conducting a risk assessment and implementing a quality control plan. A revision of CLSI EP23-A is currently being drafted, and this presentation will preview a few of the updates that can be expected in the next version of the guidance document.

SP03 - Diagnostica decentrata di COVID-19: rischi e opportunità

SP03-01

TESTING FOR SARS-COV-2: SELF-SAMPLING AND PRE-ANALYTICAL ISSUES

A. Padoan

Department of Medicine, DIMED, University of Padova and Department of Laboratory Medicine, University Hospital of Padova, Italy

Although reverse real-time PCR (rRT-PCR) remains the gold standard for detecting SARS-CoV-2, high tests demanding has overwhelmed molecular laboratory capacities in all countries around the world, especially during early pandemics. During the second wave, the validation of SARS-CoV-2 antigen rapid diagnostic tests (RDT) has substantially changed testing strategies globally, since results were available within 30 min, reducing turnaround time and therefore exposure risk. Recently, validated self-tests for SARS-CoV-2 based on the

nasopharyngeal swab (NPS) or saliva have prompted for the empowerment of the general population in the fight against the spread of infectious.
Swabbing is a complex task requiring training and competency assessment, and thus they are performed by trained nurses or physicians. The complexity of NPS, coupled with a lack of a standard swabbing practice may contribute to a high number of false-negative results for SARS-CoV-2. SARS-CoV-2 rRT-PCR false-negative results have been reported to be as high as 41% and several reports exist of patients negative to NPS, who are subsequently positive on repeat testing [1]. Differently, the false-positive ratio for the SARS-CoV-2 molecular test is expected to be very low, since PCR design is mostly unaffected by false-positive results. Recently, Tsang et al. compared the diagnostic performance of different clinical specimens, including nasopharyngeal, nasal, throat, and oropharyngeal swabs and saliva and they found that using NPS as the gold standard, moderate sensitivities were achieved by saliva (85%, 75–93) and nasal swabs (86%, 77–93) and a much lower sensitivity by throat swabs (68%, 35–94). The Authors concluded that saliva and nasal swabs are clinically acceptable alternatives to commonly used nasopharyngeal swabs. Saliva is a matrix elective for self-collection, and molecular testing is reliable but require laboratory instrumentation to be performed. Indeed, antigen determination on salivary samples is still under debate [2].
Most of the errors occur in the preanalytical phase, with relatively few analytical and post-analytical errors. Some issues arising during the pre-analytical phase of SARS-CoV-2 diagnostics regards: the time of swab, swabbing practice, sample handling and conservation and RNA extraction. NPS should be taken at the time of symptom onset when the highest viral load occurs in COVID-19, thus not the day immediately before (and not too far from) possible close contact with positive subjects. Sample handling and storage were only partially a limiting factor when samples are kept a 4 °C and processed within 5 days [2]. Differently, sample preparation is a crucial factor for antigen testing, and centrifuged vs non-centrifuged samples give discordant results.
In conclusion, self-testing could be of aid in the screening programs for reducing viral spread, but other alternatives are possible, such as self-collection of samples with analytical tests performed in clinical laboratories. These required the optimization of pre-analytical steps to reduce the impact on results.

REFERENCES

1. Woloshin, S.; Patel, N.; Kesselheim, A.S. False Negative Tests for SARS-CoV-2 Infection — Challenges and Implications. N. Engl. J. Med. 2020, 383, e38.
2. Basso, D.; Aita, A.; Navaglia, F.; Franchin, E.; Fioretto, P.; Moz, S.; Bozzato, D.; Zambon, C.-F.; Martin, B.; Dal Prà, C.; et al. SARS-CoV-2 RNA identification in nasopharyngeal swabs: issues in pre-analytics. Clin. Chem. Lab. Med. 2020, 58, 1579–1586.

SP03-02

DECENTRALIZED COVID-19 DIAGNOSTICS: RISKS AND OPPORTUNITIES. RAPID SEROLOGICAL TESTING

G. Lippi

Section of Clinical Biochemistry, University of Verona, Verona, Italy

The knowledge that has been garnered so far on severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection is that humoral immunity encompasses the generation of immunoglobulins of most classes against surface viral antigens, which mostly involve the spike protein, the nucleocapsid protein, but also envelope and membrane proteins. Since the spike protein is the anchor that the virus uses for penetrating the host cells through biding with its natural host cells receptors, it can be assumed that antibodies binding to spike protein of SARS-CoV-2, and especially to its receptor binding domain, would retain stronger neutralizing potency against the virus. Serological testing has been conventionally defined as a diagnostic procedure used for detecting an immune response against an infectious agent. This definition shall dissipate any residual doubt about the fact that this type of testing is not intended to replace the identification of viral RNA for diagnosing SARS-CoV-2 infection, but must be rather used for establishing if individuals have been infected by the virus and/or have developed an immune response. The diagnostic sensitivity stratified according to the assay methodology is highly variable. Recent evidence confirms better performance for chemiluminescent and ELISA anti-SARS-CoV-2 IgG immunoassays compared to lateral flow immunoassays, whose sensitivity remains far below 80%. Additionally important drawbacks of rapid serological tests include the facts that the information provided by the companies is concerning because often lacks details, its quality is considerably variegated among different devices, several claims are vague, there is a lack of transparency along with the fact that human aspects are not been adequately addressed for purpose of alleviating the risk of inappropriately using the device. The risk of misinterpreting tests results by patients when rapid kits are used for self-diagnosis is another aspect that must be considered. Recent evidence was provided that over 2% of patients may misdiagnose themselves as being negative while the device generates positive results. This was mostly due to objective difficulties encountered by the patients in reading and interpreting the results of the strips. Important considerations for implementing point-of-care serology testing thus include (i) usage of well-validated tests, evaluated against a gold standard; (ii) performance characteristics - thus encompassing sensitivity, specificity, positive and negative predictive values or cross-reaction with other coronaviruses - shall be tested using serum samples collected from patients infected with SARS-CoV-2, with other respiratory viruses (including seasonal coronaviruses) and also from healthy controls; (iii) adequate training of healthcare workers is needed (iv) and, finally, (IV) provisions must be in place, encompassing the capture of testing data for individual patient records and surveillance purposes, and the participation to external quality assessment schemes, to systematically monitor the quality of this type of testing.

SP03-CO07

DETERMINATION OF SARS-COV-2 ANTIBODIES IN SALIVARY SAMPLES FROM VACCINATED INDIVIDUALS AND COVID-19 PATIENTS

C. Cosma[1], A. Padoan[1], C. Di Chiara[2], D. Rinaldi[1], D. Donà[2], A. Gastaldi[3], D. Basso[1], C. Giaquinto[2], M. Plebani[1]

[1]Department of Laboratory Medicine, University-Hospital of Padua, Italy
[2]Division of Pediatric Infectious Diseases, Department for Women's and Children's Health, University of Padua, Italy
[3]Department of Pediatrics, Woman and Child Hospital, University of Verona, Verona, Italy

Background and Aim: Salivary SARS-CoV-2 Ab determination could be suitable for monitoring the viral spread and vaccination efficacy, especially in pediatric patients. We investigated N/S1-RBD IgG antibody levels in salivary samples of infectious-naïve vaccinated subjects and of COVID-19 patients, further comparing levels with serum anti-SARS-CoV-2 S-RBD IgG.
Methods: A total of 72 subjects were enrolled at the Padova University Hospital: 36 COVID-19 patients and 36 health care workers (HCW), who underwent a complete vaccination campaign with BNT162b2 (BioNTech/Pfizer). All collected a salivary sample, using Salivette (Sarstedt, Nümbrecht Germany). For 9 HCW, salivary samples were collected at three different times within the same day (before breakfast, at 10 am, and after lunch). A serum sample was also collected for all individuals. Time post symptoms onset or time from the first vaccine were also recorded. Salivary COVID-19 N/S1 RBD (sal-IgG) ELISA (RayBiotech, GA, USA) and anti-SARS-CoV-2 S-RBD IgG Ab (ser-IgG) (Snibe Diagnostics, Shenzhen, China) were used for determining IgG Ab.
Results: Subjects' mean age (±sd) was 35.8±18.2 yrs. Age significantly differed ($p<0.001$) from COVID-19 patients [29.7±17.3 yrs] and HCW [47.1±12.9 yrs]. Positive sal-IgG were found in 70/72 (97.2%) samples; in sera, 71/72 (98.6%) samples were positive to ser-IgG. The sal-IgG median levels differed from COVID-19 to vaccinated HCW, being in salivary samples 0.21 kAU/L and 0.8 kAU/L ($p =0.030$), respectively; median levels for ser-IgG in COVID-19 and vaccinated HCW were 135 kBAU/L and 940 kBAU/L, respectively ($p<0.001$). Salivary IgG levels were not influenced by time post-symptom onset or time post-vaccination, both on vaccinated HCW (rho= -0.147, $p=0.402$) and COVID-19 subjects (rho=0.0267, $p=0.986$). Ser-IgG levels was not influenced by the time post-symptom onset for COVID-19 subjects (rho=0.102, $p=0.419$), while a strong significant correlation was found with time post-vaccination in HCW (rho=-0.6292, $p<0.001$). Sal-IgG levels were not-influenced by the daytime of collection (rho=0.148, $p=0.373$). Passing-Bablok regressions showed that sar-IgG and ser-IgG comparability was assessable only when ser-IgG values were divided by 1000, being slope and intercept 0.068 (95%CI: 0.069-0.341) and 0.221 (95%CI:-0.097 to 0.786), respectively. Conclusions: Salivary IgG is efficiently detectable both in COVID-19 and in vaccinated individuals and analyses appeared to be not influenced by the daytime of collection. The analyses performed showed that, overall, sal-IgG were lower than ser-IgG, and thus comparability with serum levels needs to be better explored.

SP03-CO08

MDW IS A NOVEL INFLAMMATORY BIOMARKER WITH PROGNOSTIC RELEVANCE IN COVID-19 PATIENTS

G. Riva[1], V. Nasillo[1], A.M. Ottomano[1], G. Bergonzini[1], A. Paolini[2], B. Lusenti[1], S. Castellano[1], R. Rizkallah[1], P. Ferrari[1], M. Varani[1], M. Luppi[2], E. Tagliafico[1], T. Trenti[1]

[1]Dip. Int. Interaz. Medicina di Laboratorio e Anatomia Patologica, AOU/AUSL di Modena, Italy
[2]UO Ematologia, Univ. Modena e Reggio Emilia, AOU di Modena, Italy

Monocyte Distribution Width (MDW), a new hematologic parameter correlating with cytomorphologic changes occurring during monocyte activation, has recently been described as promising early biomarker of sepsis. Similar to sepsis, in SARS-CoV-2-associated disease (COVID-19), monocyte/macrophage subsets are considered key mediators of the life-threatening hyperinflammatory disorder –commonly defined as 'cytokine storm'– which is part of the complex infectionassociated immune dysregulation observed in severe COVID-19 cases (possibly, representing a new kind of viral sepsis). Thus, we aimed at investigating possible prognostic roles of MDW testing during monitoring of COVID-19 patients.In this work, we longitudinally measured MDW values in a cohort of 87 patients with molecularly-proven COVID-19 diagnosis, consecutively admitted to our intensive/subintensive clinics in early 2020. Statistical analyses were applied to correlate MDW values with common inflammatory markers, disease severity, clinical trajectories and final outcome.We found significant direct correlations between MDW and different inflammatory markers routinely assessed during hospitalization, namely CRP ($p<0.001$), fibrinogen ($p<0.001$) and ferritin ($p<0.01$). Moreover, high MDW values were remarkably associated with fatal outcome (AUC=0.76, sensitivity 0.75, specificity 0.70, MDW threshold 26.4; RR=4.91, OR=7.14). Furthermore, evaluating MDW dynamics in cases with longer followup, we frequently observed progressive MDW increments in patients with worsening inflammatory conditions, while clinical recoveries were consistently associated with MDW decreases.Our study shows, for the first time, that MDW can be useful in the prognostic monitoring of hospitalized COVID-19 patients, as it is: (i) easy and rapid to obtain, (ii) directly related to the activation state of a fundamental inflammatory cell subset (i.e. monocytes, pivotal both in cytokine storm and in sepsis immunopathogenesis), (iii) strongly correlated with clinical severity of COVID-19- associated inflammatory disorder, and, in turn, (iv) endowed with relevant prognostic significance. Additional studies are needed to define the role of MDW monitoring in other clinical settings, including COVID-19 outpatients.

SS08 - Young Scientists - Evoluzione della Medicina di Laboratorio: strategie e nuove sfide

CJ01

LABORATORY MEDICINE WOULD MERIT A FURTHER SMALL REVOLUTION

F. Salvatore

Professor of Human Biochemistry, Emeritus
Dipartimento di Medicina Molecolare e Biotecnologie Mediche
Università di Napoli Federico II
CEINGE-Biotecnologie Avanzate
Founder and Principal Investigator
Past (president and scientific coordinator)
Member of Accademia Nazionale delle Scienze (detta dei XL) - Roma

In the last couple of decades, Laboratory Medicine has made giant steps forward in terms of innovative technology and has made major scientific breakthroughs in the medical field as a whole. Indeed, a plethora of both in vitro and in vivo assays and tests in biological fluids of the human hydrodynamic system are now available.
The importance, for clinical purposes, of novel metabolic processes and protein cross-talk mechanisms is being increasingly recognized. The increased survival period of sick, elderly people, plus the therapeutic aspects of precision medicine, in which the drugs selected resulted in a series of direct approaches to altered target molecules, have made it difficult to identify the most effective molecules to use as biomarkers in most of this population scenario.
In this optics, the clinical value of Laboratory Medicine has now reached about 70% of the most important measures used to diagnose diseases, but at a cost to the National Health System of many countries that reaches a maximum of 5% of the global health costs. Therefore, it seems that Laboratory Medicine does not need to increase further value in the contribution to the care of fragile individuals, and in people affected by chronic degenerative diseases.
Notwithstanding all these premises, and the increase in Clinical Laboratory testing, which is, and will continue in the future to be an indispensable ally of medical care, the correct diagnosis of a single or of multiple diseases occurring in a single individual will benefit enormously from this Discipline, if some steps forward will be made. I believe that the enormous amount of knowledge now accumulating in the field of Laboratory Medicine will revolutionize, not only the medical care of people, but, in the various areas of the medical scenario, also the field of Laboratory Medicine Science itself and the practice deriving from it.
However, there is a grey, largely neglected area in humankind: although life-span has almost doubled in the last 150 years, I believe the time has come to look at the wellbeing of each individual during his/her lifespan, particularly because multimorbidity occurs during the lifetime of each individual. In other words, we should all begin to be mindful of our state of health as early as about 20-25 years of age, when most auxological aspects have been reached, and sexual maturity completed. Consequently, I believe that each person should start a “health diary” at that age. Therefore, also healthy people should be monitored as well as patients , which should be one of the tenets of preventive medicine Having said that, I must now say that chronological age is practically meaningless in calculating health status. In fact, only a very careful analysis of an individual’s personal functional and morphological aspects will reveal early signs of disease, and enable physicians to prevent its progression. This, of course, applies much more to multimorbidity; in fact, once identified them, measures can be made to eradicate or to delay the start or the progression of each illness, therefore determining a better state of health during the progression of chronological age.
All this would revolutionize today’s medicine where the physician looks for early signs and symptoms of each possible alteration/disease, before deciding on treatment. The revolution I am talking about is to look at each individual when they are enjoying still normal health, as mentioned above. Indeed, current practice will become to measure a large series of functional laboratory parameters relating to all the functional assets of single tissues and/or organs, and also by imaging assessment, namely by looking at the morphological aspects of all the organs and tissues of the human body, mainly using echography approaches, and also by making a total body scan of different parts of the organism, and this, as said before, starting very early, i.e ,at 20-25 years old.
This approach may be considered too costly, but in effect it is much less costly than waiting for the appearance of an overt disease, which must then be treated for decades, frequently with very expensive drugs and tests (laboratory and imaging).
In this short presentation, I’ll also discuss theoretical and practical methods that can be used in the practice of predictive medicine at genomic level, as well as secondary preventive aspects aimed at improving the health of each individual, taking into consideration the primary prevention of diseases, also by decreasing environmental nocive factors, and tailor beneficial personal life style approaches for each person.
The inversion of the “paradigm” between aging and disease (1), the misnomers of the use of the term “age-associated disease”, and other considerations related to ideological aspects of so-called oxymoron term, physiological aging, are discussed to illustrate the need for this expected revolution in medical care, including Laboratory Medicine approaches. This will also support the joining of Preventive Medicine to effective Individualized Medicine.

REFERENCES

1. Salvatore F. The shift of the paradigm between ageing and diseases. Clin Chem.Lab Med. 2020 Sep 25;58(10):1635-1644. doi: 10.1515/cclm-2020-0125. PMID:32286241.

CJ02

DRIVE THROUGH DIFESA: L’ITALIA DIVENTA AREA DI CRISI

C. Renzi

Policlinico Militare - Roma

Con l'avvio dell'Operazione IGEA, la Difesa ha fornito il suo supporto al Servizio Sanitario Nazionale per l'attività

di screening del Coronavirus mettendo a disposizione della Nazione circa 200 postazioni distribuite su tutto il territorio nazionale. Ad oggi sono operativi circa 72 Drive-Through-Difesa. I contributi, forniti da ciascuna Forza Armata, sono diretti e coordinati fin dalla prima ora dal Comando Operativo di vertice Interforze (COI) per mezzo di una Sala Operativa dedicata, composta da personale interforze. In aggiunta al Policlinico Militare di Roma "Celio" sono stati inoltre messi a disposizione anche ulteriori 11 laboratori in tutta Italia e sono già stati eseguiti ben oltre 2,9 milioni di tamponi. Il concorso della Difesa nel contrasto al COVID 19 ha visto impegnati dal 23 ottobre 2020 circa 1.895 militari al giorno, per un totale di 434.107 giornate/uomo complessive. Con l'arrivo delle prime dosi di Vaccino, su richiesta della Struttura Commissariale, il Comando di Vertice Interforze della Difesa ha avviato l'Operazione EOS e, facendo tesoro dell'esperienza e delle specifiche competenze logistiche acquisite in questi anni di impegno nelle varie missioni nei diversi Teatri Internazionali, ha approntato e implementato un piano di distribuzione delle dosi mettendo a disposizione un dispositivo, prontamente adattabile in base alle esigenze, composto da 11 aerei, 73 elicotteri e 322 mezzi. Nel valutare alcune richieste pervenute dalle ASL, la Difesa ha successivamente convertito i Drive Through in "presidi per la somministrazione dei vaccini"(PVD), attività questa che si è aggiunta a quella già in atto, di stoccaggio dei vaccini presso l'aeroporto di Pratica di Mare e il successivo trasporto in tutte le regioni italiane. Ad oggi sono stati attivati sul territorio nazionale 30 Presidi Vaccinali della Difesa che supportano la Sanità Nazionale con le vaccinazioni a favore della popolazione civile, i quali hanno eseguito già oltre 473 mila vaccinazioni. Ad essi si aggiungono i 35 Presidi Vaccinali Mobili della Difesa con il compito di supportare la campagna vaccinale soprattutto in quelle località più difficili da raggiungere, che hanno eseguito oltre 53 mila vaccinazioni. È stata avviata inoltre la campagna vaccinale a favore delle isole minori tra cui le Tremiti, le Eolie, Pantelleria, Ustica, le isole della regione Sardegna, l'isola di Capraia e del Giglio, per le quali sono state somministrate oltre 25 mila vaccinazioni. Preziosissimo il contributo del Policlinico Militare "Celio", uno dei tre Ospedali Militari di riferimento, che è stato riconvertito in tempi rapidissimi in Covid Hospital ed inserito nella rete nazionale anti Covid quale riferimento delle strutture sanitarie del Centro Italia, mettendo a disposizione 152 posti letto di cui 100 di degenza ordinaria e 52 di sub-intensiva/intensiva.

CJ03

TRATTAMENTO DEI DATI SANITARI: PROGRESSO SCIENTIFICO E PRIVACY

V. Notarangelo

Data Protection Officer & Legal Counsel nei settori banking e sanità".

Al centro della società 4.0 ci sono i dati, che sono il motore di tutto e, per mezzo di essi, si muovono il progresso, l'economia e, oggi più che mai, la sanità e la ricerca scientifica.
È in tali settori che, ultimamente, si sono registrati i maggiori investimenti nella digital transformation finalizzata a sfruttare -attraverso i dati- tutte le nuove tecnologie presenti ed emergenti, dall'Internet of Things (IoT) all'Artificial Intelligence (IA). Lo sfruttamento dei Big Data, di fatto, costituisce il punto di partenza e la risorsa indispensabile per lo sviluppo della medicina innovativa e di precisione, fornendo supporto scientifico, organizzativo e infrastrutturale per promuovere la ricerca ed accelerare gli studi preclinici e clinici.
Tale sviluppo, tuttavia, avendo aumentato il numero dei soggetti che detengono dati relativi alla salute, la velocità di trasmissione di tali dati e la quantità delle informazioni elettronicamente archiviate (spesso non in territorio nazionale), ha determinato un aumento esponenziale della pericolosità dei trattamenti di dati dal punto di vista della riservatezza e un'accresciuta possibilità di ledere la dignità e le libertà fondamentali della persona. Ne è conseguita un'accentuata sensibilità del legislatore europeo e, a seguire, di quello nazionale, nei confronti della tutela di tali dati e tutele connesse. Oltre al Regolamento Europeo sulla Protezione dei Dati, che ha rivoluzionato il modo di concepire la data economy, è, infatti, in corso di valutazione -da parte delle istituzioni europee- la prima bozza di Regolamento sull'Intelligenza Artificiale, che costituirà il vero trampolino di lancio all'utilizzo massivo e regolamentato degli algoritmi, soprattutto in ambito healthcare.
Per la verità, tale ultima normativa citata, non farà altro che definire gli argini all'utilizzo di sistemi algoritmici già ampiamente in uso. Ne è una prova il recente intervento[1] dell'Agenzia Italiana del Farmaco (AIFA), che ha inteso richiamare e sottolineare tutte le normative da rispettare ai fini della presentazione e della conduzione di sperimentazioni attraverso algoritmi e tecniche di Machine Learning. L'AIFA, mediante tale guida, ha descritto alcuni case study, mostrando alcuni workflow che rappresentano le norme impattate a seconda della tipologia di sistema utilizzato e ponendo particolare attenzione alla compliance legata al trattamento dei dati e ai profili connessi di cybersecurity.
La sfida nell'utilizzo dei dati sanitari con applicazione di sistemi di AI in sanità e nella ricerca scientifica è, dunque, quella di trasformare la "consueta" classificazione di una malattia in un migliore processo decisionale clinico, definendo più precisamente le caratteristiche e i contorni che la singola patologia evidenzia nel caso di specie, per poi ottenere – grazie ad algoritmi e processi di machine learning – protocolli di cura specifici, personalizzati, eventualmente predittivi.

1. AGENZIA ITALIANA DEL FARMACO (AIFA), Guida alla presentazione della domanda di autorizzazione alla Sperimentazione Clinica che preveda l'utilizzo di sistemi di Intelligenza Artificiale (AI) o di Machine Learning (ML), 24.05.2021 https://www.aifa.gov.it/

SS09 - CASI CLINICI selezionati da abstract

CC001

Utilità dell'analisi genetica nel tumore del testicolo

M. Nunziato[1,2], F. Di Maggio[1,2], G. Damaggio[3], F. Crocetto[4], S.D. Pandolfo[4], A. Aveta [4], A. Calabrese[5], C. Imbimbo[4], V. Colonna [3], F. Salvatore[1,2]

[1]Ceinge-Biotecnologie Avanzate,Naples, Italy

[2]Department of Molecular Medicine and Medical Biotechnologies, University of Naples Federico II, Naples, Italy

[3]Institute of Genetics and Biophysics "A. Buzzati-Traverso", National Research Council (CNR), Naples, Italy

[4]Department of Neurosciences, Human Reproduction and Odontostomatology, University of Naples Federico II, Naples 80131, Italy

[5]Istituto Nazionale Tumori IRCCS "Fondazione G. Pascale", Via Mariano Semmola, 53, 80131 Napoli NA, Italy

Testicular cancer (TC) is a rather common neoplasia in men; the incidence in 2020 worldwide was 74.458, and the mortality accounts for about 12%. In this context, the early diagnosis and the comprehension of genetic pathogenesis gain an important role. A 18 years old patient was enrolled for a neoformation of the left didymus; he underwent an orchifunicolectomy of the left testicle. The histological diagnosis indicated mixed germ cell tumor consisting mainly of embryonic carcinoma (~80%) with a share of teratoma (~15%) and a share of Yolk-Sak tumor (~5%). Due to the early-onset and familiarity for seminoma (father, onset at 40 ys), we performed, firstly, a genetic analysis on the family-trio using our customized 48 multi-gene panel, which accounts for 883 target regions and includes all coding regions/gene and some adjacent noncoding regions. The 48 genes selected are associated to various typology of cancer as colon, prostate, breast and ovarian ones. The libraries have been obtained using the HaloPlex Target Enrichment System (Agilent Technologies). Sequencing run was performed using MiSeq platform (Illumina) and data analysis for variants identification was performed using Alissa Software. The average read depth obtained, was 511X, 515X and 605X for the proband, his father and his mother, respectively. We identified, two interesting variants: one shared with his mother in CHEK2, c.721+3A>T, reported as conflicting for pathogenicity in ClinVar database, and one de novo in ELAC2, c.2389G>T (p.Glu797Ter), predicted as Likely Pathogenic with in silico analysis.Then, we extended the analyses to Whole Genome Sequencing (WGS) using the Oxford Nanopore Technology (ONT) that allows both, (i) genome comparison between the trio and (ii) whole methylome analysis. The libraries have been prepared without fragmentation step (Ligation Sequencing Kit, Nanopore Oxford). Three different sequencing runs, for each patient, were performed on Promethion-24. The bioinformatics analysis was performed using Deep Variant for variant calling, Nanopolish and PycoMeth for methylome analysis.Comparison of the methylation profile, among the members of the trio, in 1.8M windows of the genome (size 500bp), revealed 260 windows with significant differences in methylation (p-value<0.01). Overall, the father and the child genome are less methylated compared to the mother. Interestingly, a 607kb region on Chromosome 20 (GRChg38) is significantly unmethylated in the father and the child compared to the mother. In conclusion, with the Nanopore approach, in a single step strategy we can obtain all the information for a complete first glance characterization of the genomic sequencing profile.This work is supported by CIRO project (to FS) from Campania Region (Italy), SATIN “Neoplasia studies” from Campania Region (to FS) and “Predictive Medicine in neoplasia” (to FS) from Campania Region (Italy).

CC002

Tre casi di possibile tossicità da farmaci

R. Simeoli[1], S. Cairoli[1], D. Cocciadiferro[2], E. Agolini[2], M. Marano[3], L. Lancella[4], L. Cursi[4], A. Vitale[1], V. Ventura[1], G. Antonetti[1], B.M. Goffredo[1]

[1] 1Department of Pediatric Specialties, Division of Metabolic Biochemistry, Children's Hospital Bambino Gesù, IRCCS, Rome, Italy;

[2] 2Laboratory of Medical Genetics, IRCCS, Children's Hospital Bambino Gesù, IRCCS, Rome, Italy;

[3] 3Pediatric Poison Control Center, Children's Hospital Bambino Gesù, IRCCS, Rome, Italy;

[4] 4Pediatrics and Infectious Diseases Unit, Children's Hospital Bambino Gesù, IRCCS, Rome, Italy;

Introduction: Therapeutic Drug Monitoring (TDM) is defined as the measurement of drug plasma concentrations at a specific time in a dosing interval. This application is particularly useful in pediatric patients where drug metabolism is often affected by developmental changes resulting in more variable plasmatic levels compared to adults. Variability in drug response may be caused by genetic polymorphisms, therefore in order to obtain a personalized medicine approach, TDM can be combined to Pharmacogenetics (PGx) tests especially when cases of altered drug responses or toxicity are reported.

Methods: Using Liquid Chromatography associated to Mass Spectrometry (LC-MS/MS), we routinely analyze plasmatic concentration of several drugs. In addition, Laboratory of Medical Genetics is able to run a Next Generation Sequencing (NGS) gene panel in order to evaluate presence of genetic variations or single nucleotide polymorphisms (SNPs) in genes encoding for proteins involved in drug metabolism and transport.

Results: During TDM routine, when analysis of plasma concentrations are above the laboratory alert values and patients presented signs of toxicity, PGx tests were performed. We described three clinical cases of patients with clinical signs of toxicity due to Phenytoin (PHT), Isoniazid (INH) and Voriconazole (VO) accumulation, respectively. Analysis of plasma concentrations confirmed levels above the laboratory alert values for Phenytoin, Isoniazid and Voriconazole. PGx tests were performed for these patients revealing for PHT patient, the homozygous variant c.1075A>C (p.Ile359Leu) in the CYP2C9, corresponding to the CYP2C9*3 haplotype, while the NAT2*5C/6B haplotype was identified in the INH patient. Therefore, patients were classified as poor metabolizer for PHT and INH, respectively. Similarly, patient treated with VO showed the variant NM_000769.2 (CYP2C19): c.681G>A; p.Pro227Pro, corresponding to the CYP2C19*1/*2 haplotype classifying this patient as intermediate metabolizer.

Conclusions: These cases show that TDM combined with PGx could help clinicians during the diagnostic process. In particular, this approach can be used not only for monitoring drug concentrations but also for predicting different pharmacogenetic variants accountable of altered responses to different pharmacological treatments. Therefore, combination of TDM and PGx represents a valid tool for a personalized medicine approach reducing risks of drug toxicity and/or therapeutic failures during the routine clinical practice.

CC003
Preziose informazioni dall'esame del liquido pericardico

A. Sharif Rouhani[1], F. Spanu[1], C. Ferraris Fusarini[1], M. Ammirabile[1], A.C. Migliorini[1], M. Vidali[1], G.A. Croci[2], F. Ceriotti[1]

[1]U.O.C. Lab. Analisi, Osp. Maggiore Policlinico, Milano
[2]U.O.C. Anatomia patologica, Osp. Maggiore Policlinico, Milano

Il pericardio è una membrana sottile che ricopre il cuore e la radice dei principali vasi sanguigni. È formato da due strati, separati dalla cavità pericardica, e contiene il liquido pericardico (LP, volume 20-50 ml). Si parla di versamento pericardico (VP) se il volume di LP nella cavità supera il valore normale. Il tamponamento cardiaco (TC) si ha quando un abbondante VP ostacola il riempimento delle cavità cardiache durante la diastole, con alterazioni del sistema cardiovascolare. Nell'aprile 2021, accede in pronto soccorso (PS), per dispnea ingravescente, un uomo di 63 anni fumatore, iperteso e in terapia con Rivaroxaban. Mediante ecocardiogramma si evidenzia un TC: il paziente è sottoposto a pericardiocentesi. In laboratorio arriva un campione di LP per la conta dei globuli bianchi (GB) e gli esami morfologico e chimico-fisico. Esso presenta 6800 GB/µL, con LDH, albumina e proteine rispettivamente di 3601 U/L, 2.5 g/dL e 4.80 g/dL. L'esame morfologico mostra un tappeto di emazie, granulociti neutrofili (11%), linfociti (70%) ed elementi monocito-macrofagici (19%). Si trovano, inoltre, numerose cellule di natura non ematopoietica (CDNNE) con aspetto dismorfico, risultato comunicato al PS. La TAC eseguita rileva un versamento pleurico: si preleva un campione di liquido (LPL) per le analisi. Anche il LPL mostra numerose emazie, granulociti neutrofili (3%), linfociti (45%), elementi monocito-macrofagici (52%) e CDNNE, simili a quelle di LP. Queste ultime si trovano anche nel liquido ascitico, prelevato per ulteriore presenza di versamento addominale. Alla TAC si vede una trombosi a livello dell'arteria polmonare comune, adenomegalie multiple, in particolare adenopatia in sede paratracheale e sovraclaveare. Si effettua pertanto un'agobiopsia del linfonodo sovraclaveare che consente di porre diagnosi di carcinoma polmonare scarsamente differenziato, a fenotipo citocheratina 7+/-, citocheratine 5/6+, p63+/-, compatibile con un istotipo squamocellulare. In conclusione, l'analisi di laboratorio del LP ha permesso, in tempi brevi, di dare un'indicazione ipotetica della presenza di neoplasia. Solo in tempi successivi al ricovero del paziente, e mediante altri esami, è stata confermata la presenza di una forma tumorale ormai metastatizzata.

CC004
Una diagnosi difficile in un paziente dializzato peritoneale

G. Canu[1], G. Alfano[2], S. Tagliavini[1], C. Canali[1], L. Giampaolo[1], M. Tagliazucchi[1], A.M. Ottomano[1], E. Tagliafico[1], T. Trenti[1], M. Varani[1]

[1]Department of Laboratory Medicine and Pathology AUSL-AOU Modena
[2]Nephrology, Dialysis and Transplant Unit, University Hospital of Modena

Introduction: Interleukin-6 (IL-6) is a pro-inflammatory cytokine secreted by lymphocytes, fibroblasts and macrophages involved in B-cell differentiation and stimulation of acute-phase proteins. IL-6 is associated with high serum levels in viral human infections such as hepatitis B and C virus, influenza virus, herpes simplex virus, HIV and also in coronavirus disease 2019. This cytokine is also produced by a wide array of intraperitoneal cells after the exposition to a local noxa patogena.Icodextrin has been associate with sterile peritonitis in patients on peritoneal dialysis (PD): this type of peritonitis is a cause of cloudy effluent and mild abdominal discomfort that resolved with the discontinuation of icodextrin. The diagnosis of icodextrin-associated peritonitis is critical to avoid unnecessary antibiotic prescription.Here, we described a case report of steril icodextrin-associated peritonitis coupled with elevation of IL-6 on peritoneal dialysate occurred in a male 76 years old undergoing PD.
Methods: IL-6 (DXI 800 Beckman Coulter) and leucocyte count were performed on peripheral blood sample and peritoneal dialysate before and after icodextrin rechallenge. Serum reactive C protein (PCR), serum procalcitonin (PCT) and peritoneal effluent colture were performed before and after icodextrin rechallenge.
Results: After 48 hours from the start of icodextrin rechallenge, peritoneal effluent became cloudy with a slight increase in leucocyte count (178 cells/microlitro with 11% neutrophil granulocytes, vs 62). Dyalisate colture, serum PCR and PCT resulted negative; leucocyte count in peripheral blood resulted normal (7300/µL). IL-6 level increased steeply in peritoneal effluent when compared to baseline (1124 vs 114 pg/mL) and subsided to baseline levels with the withdrawal of the icodextrin solution without increase in serum IL-6 (15.7 vs 12 pg/mL); likewise leucocyte count on peritoneal dialysate decreased (63 cells/µL).
Discussion: IL-6 can be used, along with peritoneal leukocyte count, as a precocious and sensitive marker of local inflammation and, in these cases, to discriminate from non-inflammatory peritonitis.
Reference: Yang X, Tong Y, Yan H, et al. High Intraperitoneal Interleukin-6 Levels Predict Peritonitis in Peritoneal Dialysis Patients: A Prospective Cohort Study. Am J Nephrol. 2018;47(5):317-324

CC005
Due pazienti fragili in Pronto Soccorso

M. Casini[1,2], T. Pavia[1], V. Guerri [1,2], M. Martelloni [3], L. Macchia[3,2], B. Fedi[1], C. Giusti[1], E. Gaudio[1], P. Chiarugi[1,2], G. Pellegrini[1,2]

[1]Lab. Analisi Chimico Cliniche Azienda Ospedaliero Universitaria Pisana
[2]Centro FCSA n. 281 Azienda Ospedaliero Universitaria Pisana
[3]SD Patologia Clinica Azienda Ospedaliero Universitaria Pisana

Two cases of dabigatran intoxication are suitable for our observation in recent months: they consist in two frail women both treated with dabigatran for atrial fibrillation (AF).
First case. A 68-years-old woman, accessed to the first aid for an accidental fall, non-commotional head trauma. Potus, general conditions expired, melena and rectorrhagia, anemia. Coagulation tests (done probably three days after the suspension of dabigatran) were found: Prothrombin Time (PT) 3,02, activated Partial Thromboplastin Time (aPTT) 2,45. Since dabigatran therapy is not declared, clinicians required the study of coagulation factors. All factors were moderately reduced, excepted the FVIII which was normal; the FII was significantly reduced (6%). There was a transient decrease in liver function. Suspecting previous assumption of dabigatran, laboratory doctors performed the Thrombin Time test, which was not clottable, and therefore the dabigatran resulted 658 ng/mL. Second case. A 94-years-old woman, accessed to the first aid for presyncope, anuria, asthenia and soporous state, in therapy with verapamil. Laboratory tests revealed severe anemia (hemoglobin 5,6 g/dL), creatinine 2,03 mg/dL, PT 4,97, aPTT 3,27, dabigatran 1,224 ng/mL.
Conclusions - In accordance with the guidelines of the European Heart Rhythm Association (2021 EHRA), stroke prevention in older AF patients is of great importance as stroke risk rises greatly with age. These patients have more favourable outcomes on directed oral anticoagulant (DOAC) than without it, and on DOAC than on vitamin K antagonist (VKA). Frailty, cognitive decline and risk of falling should not generally be a reason not to anticoagulate patients. However care needs to taken to minimize the risk of complications, it is crucial to ensure a structured follow-up with periodic visits, to reassess stroke and bleeding risk, to evaluate kidney and liver function, to check blood count and to measure the concentration of DOAC. Excessive DOAC plasma concentrations expose the patients to an increased risk of bleeding, This may occur when the patient has taken an overdose; also intercurrent events such as acute renal failure (especially with dabigatran) or administration of drugs with known drug-drug interaction, such as dabigatran/verapamil.

CC006
Le malattie rare richiedono approcci multidisciplinari

M. ZAGAGLIA[1,2], L. MARINELLI[1], R. MANISCALCO[4], B. BRUSCHI[3], P. COCCIA[3], D. LIGI[4], E. DAMIANI[2]

[1]Lab. Patologia Clinica, Osp. Riuniti Ancona, Ancona
[2]Dip. Scienze della Vita e dell'Ambiente, Univ. Politecnica delle Marche, Ancona
[3]U.O. Oncoematologia Pediatrica, Osp. Riuniti Ancona, Ancona
[4]Dip. Scienze Biomolecolari, Univ. Urbino Carlo Bo, Urbino

Afibrinogenemia is a rare bleeding disorder with an estimated prevalence of 1-2 per 1,000,000 people; in countries where the inbreeding rate is very high (such as in South India) the number of cases of congenital Afibrinogenemia is significantly higher.The Afibrinogenemia is an inherited disease with an autosomal recessive trait; while homozygous individuals are clinically symptomatic, heterozygotes (simple and/or compounds) usually do not show significant symptoms.In the present study, the homozygous variant IVS4 + 1G> A (c.718 + 1G> A) of Intron 4-¤ chain has been described for the first time from a genetic-molecular point of view, as the cause of Afibrinogenemia. Moreover, an in-depth biochemical study was carried out both on the proband and parents to determine whether the pro-inflammatory status was related to genetic-molecular disorders of fibrinogen.The increased levels of C-reactive protein (an acute phase protein) correlate with an increased concentration of several pro-inflammatory cytokines and a consistent lympho-monocytosis in the afibrinogenemic proband.In our knowledge, this is the first evidence describing in an afibrinogenemic proband a significant increased plasma values of the platelet-derived growth factor-beta (PDGF-¤), a growth factor involved in platelet genesis.This novel panel of cytokines could help to explain the increased thrombotic risk that patients suffering from Afibrinogenemia are subjected to, providing possible interpretations of both inflammatory and proteolytic pathways involved in the genetic anomaly of Afibrinogenemia.Although the present novel set of biochemical-molecular laboratory data should be carefully evaluated, it may open new frontiers for future clinical-medical use adding innovative biochemical-molecular biomarkers for the diagnosis of this rare genetic disease.
References:
Pieters M et al., Res Pract Thromb Haemost. 2019;3:161–172
Asselta et al., J Thromb Haemost 2006; 4: 2115–2129

CC007

Una anemia in gravidanza da indagare attentamente

G. Barberio, F. Bassetto, E. Cover, E. Gorrasi, F. Martignago, C. Mattiuzzo, A. Pegoraro, S. Zago

U.O.C. Medicina di Laboratorio, Azienda Ulss 2 "Marca Trevigiana", Treviso (TV)

L'emoglobina (Hb) Torino è una variante instabile delle catene alfa globiniche descritta la prima volta nel 1968 in una famiglia veneta abitante a Torino e successivamente segnalata in altre tre famiglie originarie del Veneto ed in un soggetto libanese nel quale è stata ipotizzata un'origine "de novo". In letteratura la Hb Torino è stata descritta talvolta associata ad anemia emolitica e splenomegalia, mentre in altri casi risultava meno sintomatica, senza essere mai stata provata tale eterogeneità fenotipica. Una donna di 29 anni, splenectomizzata, alla seconda gravidanza, è pervenuta in laboratorio per il controllo dell'anemia con una diagnosi generica fatta nel passato di anemia emolitica. Alcuni membri della sua famiglia erano stati esaminati per controllo e non mostravano particolari segni di anemia.
L'esame dell'assetto emoglobinico della probanda, mediante cromatografia ad alta risoluzione (HPLC) e successivo controllo in elettroforesi capillare (CE), ha fornito profili "normali" con indici eritrocitari variabilmente e moderatamente diminuiti. La quantificazione della Hb A1c (12 mmoli/moli) e della Hb A2 (1,5-2,3%), nonché la storia clinica della paziente suggerivano l'esame "in vitro" della stabilità della Hb con risultati positivi sia nella probanda che nella figlia. Lo studio strutturale mediante spettrometria di massa, successivamente confermata con l'analisi dei geni alfa, previa ricerca di difetti alfa talassemici, indicavano nella probanda la presenza di alfa talassemia (-3.7kb del) allo stato eterozigote e una mutazione T>G al nt130 del gene Alfa2, associato alla sostituzione amminoacidica Phe>Val al codone 43, corrispondente alla Hb Torino. La presenza dell'alfa talassemia associata ad una variante instabile come la Hb Torino correla con il fenotipo emolitico osservato nella probanda. L'utilizzo di metodi separativi ha rilevato valori significativamente ridotti di Hb A1c e di Hb A2 e ha quindi permesso di utilizzare risorse diagnostiche che hanno consentito di risalire alla causa della condizione emolitica. Questo caso contribuisce a fornire esempi di interazione tra difetti globinici fenotipicamente rilevanti, consente di capire come pervenire a diagnosi differenziali più corrette e come risulta utile poter disporre comunque di metodi dedicati che consentano di risalire alle caratteristiche globiniche anche mediante la quantificazione della Hb A1c.

CC008

Importanti informazioni dall'esame dello striscio periferico

M. Lorubbio, P. Anedotti, C. Artini, F. Cinci, S. Di Mario , S. Fabbroni, C. Gatteschi, L. Giannotti, F. Pulcinelli, E. Tripodo, A. Ognibene

Clinical Chemical Analysis Laboratory, San Donato Arezzo Hospital

Introduction: Rarely, platelets can interact with other blood elements, forming platelet aggregates. This paper presents an isolated case of platelet satellitism around neutrophils, lymphocytes and monocytes with platelet phagocytosis by both neutrophils and monocytes.
Case presentation: The subject was an 89-year-old woman with breast cancer on anti-estrogenic hormone cancer therapy. Whole blood sample collected in a tube with K2EDTA (Ethylenediaminetetra-acetic acid) anticoagulant was analysed within 4 hours, using an XN haematology analyser (Sysmex). The CBC (complete blood count) presented the following results: WBC (White blood cell) 4.0 x 10^9/L, RBC (Red blood cell) 3.58 x 10^12/L, haemoglobin 116 g/L, haematocrit 34.9%, MCV (Mean corpuscular volume) 97.5 fL, MCH (Mean corpuscular haemoglobin) 32.5 pg, MCHC (Mean corpuscular haemoglobin concentration) 33.2 g/dL, RDW (Red blood cell distribution width) 14.6% and PLT (Platelet) 136 x 10^9/L.
Conclusion: This case report describes the platelet satellitism around neutrophils, lymphocytes and monocytes and the interesting, very rare and singular phenomenon of platelet phagocytosis by not only neutrophils but also monocytes.