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Mini-Review

Blood Sample Transportation by Pneumatic Transportation Systems: A Systematic Literature Review

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BACKGROUND: Pneumatic transportation systems (PTSs) are increasingly used for transportation of blood samples to the core laboratory. Many studies have investigated the impact of these systems on different types of analyses, but to elucidate whether PTSs in general are safe for transportation of blood samples, existing literature on the subject was systematically assessed.

METHODS: A systematic literature review was conducted following the preferred reporting items for systematic reviews and metaanalyses (PRISMA) Statement guidelines to gather studies investigating the impact of PTS on analyses in blood samples. Studies were extracted from PubMed and Embase. The search period ended November 2016.

RESULTS: A total of 39 studies were retrieved. Of these, only 12 studies were conducted on inpatients, mainly intensive care unit patients. Blood gases, hematology, and clinical chemistry were well investigated, whereas coagulation, rotational thromboelastometry, and platelet function in acutely ill patients were addressed by only 1 study each. Only a few parameters were affected in a clinically significant way (clotting time parameter in extrinsic system thromboelastometry, pO_2 in blood gas, multiplate analysis, and the hemolysis index).

CONCLUSIONS: Owing to their high degree of heterogeneity, the retrieved studies were unable to supply evidence for the safety of using PTSs for blood sample transportation. In consequence, laboratories need to measure and document the actual acceleration forces in their existing PTS, instituting quality target thresholds for these measurements such as acceleration vector sums. Computer modeling might be applied to the evaluation of future PTS installations. With the increasing use of PTS, a harmonized, international recommendation on this topic is warranted.

As a consequence of increasing fiscal demands and a concomitant wish to expedite triage of patients, not only in the intensive care unit (ICU)[4] but also in regular hospital wards, rapid blood sampling and sample transportation have received increasing attention. Use of pneumatic transportation systems (PTSs) has expanded to facilitate transport of blood samples as rapidly and cost-effectively as possible to the core laboratory.

All phases of sample handling can theoretically affect sample quality and thereby influence test results. Knowledge of and interest in those aspects that can affect preanalytical sample handling including sample transportation are growing rapidly and have led to many investigations of the impact of sample transportation by PTS on different analyses, e.g., coagulation, blood gases, and clinical chemistry. Given the large number of transportation systems, the vast number of tests, and many different approaches to investigate this topic, an overview of the research conducted in this area will provide relevant information to know what aspects have been covered and which areas still need attention.

A systematic literature review following the preferred reporting items for systematic reviews and meta-analyses (PRISMA) reporting guidelines *(1)* was conducted to gather existing knowledge within the area and to elucidate whether use of PTSs in general is safe for transportation of blood samples. For this, the PICOS system was used, i.e., with specified criteria for population, interventions, comparators, outcomes, and study design *(2)*.

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[4] Nonstandard abbreviations: ICU, intensive care unit; MeSH, medical subject headings; PTS, pneumatic transportation system; ROTEM, rotational thromboelastometry; PICOS, population, intervention, comparators, outcome, study design; PRISMA, preferred reporting items for systematic reviews and metaanalyses.

Materials and methods

ELIGIBILITY CRITERIA

Studies were eligible if the following PICOS criteria were fulfilled:

"Population" was restricted to blood samples transported by PTS. There were no demands on "Intervention." "Comparators" included standard transportation (manual) or circumstances in which samples were not transported at all, while "Outcome" was any statistical or (if available) clinically significant difference between the analyses performed in the 2 sets of samples. Finally, the "Study design" was prospective or retrospective, excluding any metaanalysis studies.

REPORT CHARACTERISTICS

Only studies written in English were included, while there were no limitations on age of the publication or the journal status (i.e., no requirements regarding the impact factor).

SEARCH STRATEGY

Studies investigating the impact of PTSs on biochemistry analysis (clinical chemistry, hematology, coagulation, blood gases) in blood samples were extracted from PubMed and Embase. The search period ended November 2016. The content of the 2 databases is very different: Whereas PubMed primarily focuses on medical science, Embase also contains a high number of studies on other types of biological science as well as social sciences. Therefore, the search strategies had to be different to avoid inclusion of too many nonmedical publications from the Embase library.

The search strategy for PubMed was as follows: ["blood specimen collection" (MeSH) or "blood specimen collection" or "blood sample" or "blood"] and ("pneumatic tube system" or "pneumatic tube conveyor" or "pneumatic dispatch" or "pneumatic tube transport") and "English language."

The search strategy for Embase was as follows: ("pneumatic tube transport" or "pneumatic tube system") and ("exp blood sampling" or "blood sampling "or "blood samples") and "blood collection specimens" and "English language."

STUDY SELECTION

All investigators participated in the further study selection, and the following information was extracted from the included studies: participant information, inclusion criteria, parameters of comparison, outcome, and study design. Exclusion criteria were irrelevant subjects, transportation without a PTS, in vitro studies, and other publication types (reviews, editorials, and case reports; Fig. 1). Importantly, studies on transportation of blood products (e.g., pooled erythrocytes or platelets) were excluded as this was not within the scope of this study. Quality of the study design, i.e., inclusion criteria, randomization, and description of the PTS, was assessed. Information on the study population, the blood tubes used and the analyses included were gathered along with the conclusions of the studies.

Results

As shown in Fig. 1, a total of 209 papers were eligible for the study. Of these, 30 papers differed from the publication type requirements (abstracts, review, comments) and were excluded. An additional 137 papers were excluded: 104 papers that had an entirely different focus, e.g., transportation of raw materials or fuel; 17 papers that concerned transportation of blood products; and 16 papers that concerned either logistics or fiscal issues related to PTS implementation. Altogether, a total of 39 papers were extracted and are summarized in Tables 1 and 2.

PNEUMATIC TRANSPORTATION SYSTEM

The retrieved studies used several different transportation systems: 7 used Swisslog *(3, 4, 5, 6, 7, 8, 9)*; 5 used Translogic or other Swisslog-related systems *(10, 11, 12, 13, 14)*; 6 used Sumetzberger *(15, 16, 17, 18, 19, 20)*; 4, Transro *(21, 22, 23, 24)*; 2 papers, Tempus *(25, 26)*; while the remaining 6 used other types of PTSs *(27, 28, 29, 30, 31, 32)*. Of note, 9 of the papers did not specify the type of PTS investigated *(33, 34, 35, 36, 37, 38, 39, 40, 41)*.

STUDY POPULATION

As shown in Table 1, 16 of the studies only included healthy persons, while 3 studies were on outpatients *(9, 11, 25)*. Furthermore, one study considered "Patients with normal hemostasis" *(7)*, while another study was a database extraction without description of the patients *(40)*. Six of the remaining studies were conducted on highly specialized patient cohorts, namely pancytopenia with acute leukemia *(17)*, thalassemia major *(15)*, patients referred for lung function testing *(32)*, and patients scheduled for coronary angiography, elective cardiothoracic surgery, or coronary artery bypass surgery *(13, 22, 34)*. The remaining 12 studies were conducted on relevant inpatients, mainly in the ICU.

ANALYSES INVESTIGATED

As shown in Table 2, a wide variety of analyses were investigated, with hematology and clinical chemistry analyses being the most frequent. More infrequent were studies on blood gases (7), whole blood coagulation testing (6), coagulation analyses (6), and platelet function testing (6). As a rarity, the study by Kriegshäuser *(18)* only investigated the impact on circulating cell-free DNA

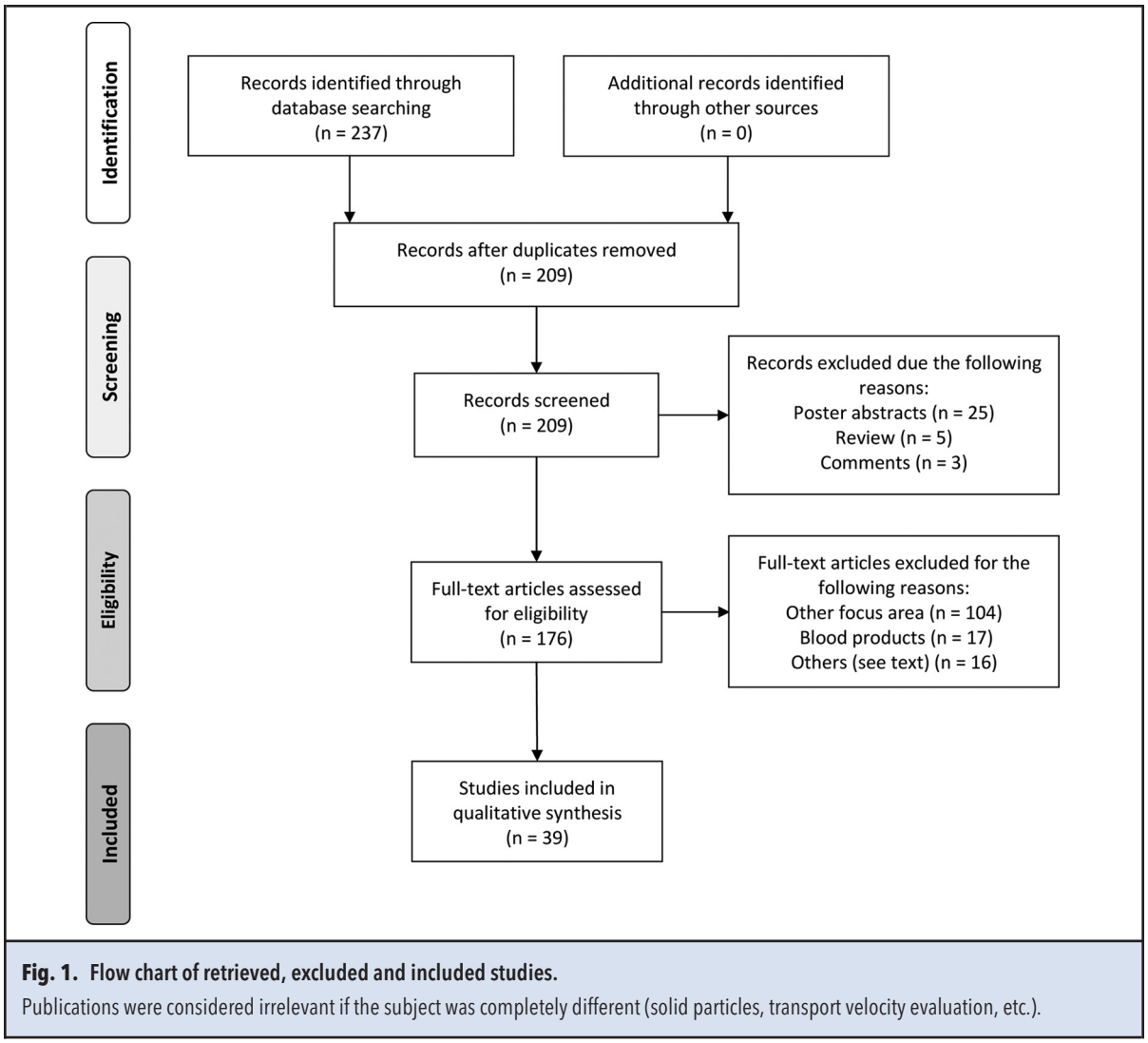

Fig. 1. Flow chart of retrieved, excluded and included studies.
Publications were considered irrelevant if the subject was completely different (solid particles, transport velocity evaluation, etc.).

in plasma. Of importance, only 1 coagulation study was on patients (samples from outpatients handled with the Tempus system) *(25)*, and only 1 rotational thromboelastometry (ROTEM) and one platelet function study were conducted on acutely ill patients *(37)*, while blood gases, hematology, and clinical chemistry were investigated in ICU patients and inpatients.

RECOMMENDATIONS GIVEN

The specific recommendations from each study are shown in Table 2.

Briefly, hemolysis index increased for most PTSs, but rarely with any clinical significance. For hematology, no differences were observed, whereas blood gas analyses in general were troublesome primarily for measurement of pO_2. For platelet function testing, results were conflicting as some studies found significant influence on multiplate platelet function testing *(22)*, while others showed that transport of correctly prepared samples produced no alterations in the results *(34)*. For whole blood coagulation testing, ROTEM parameters were influenced at higher acceleration forces *(21)*, while Glas et al. *(37)* found that only the clotting time parameter in extrinsic system thromboelastometry was affected. Finally, the study by Kriegshäuser et al. *(18)* showed no influence on circulating cell-free DNA in plasma.

Of note, all studies suggested that local testing of the PTS is necessary to ensure that samples are not affected in a way that could have a clinically significant impact. Because centrifugal or shear forces applied (in terms of acceleration vector sums and peak g-force) always rely on the local arrangement of the transportation tubes, their effects are almost impossible to predict theoretically, giving a rationale for why specific local testing is warranted.

Table 1. The studies included, with the PTSs and patient populations investigated.

Study	Pneumatic transportation system	Study population
Victor Peter *(29)*	Aerocom	Medical ICU patients
Tiwari *(30)*	Atlas	Healthy volunteers
Sodi *(31)*	Atlas system	Consenting patients
Zaman *(32)*	GCT 3000 Aerocom	Patients on pneumology wards or referred to LFT
Gossez *(27)*	HÖRTIG rohrpost	Healthy donors
Kocak *(20)*	MP10000 Sumetzberger	Healthy blood donors
Astles *(33)*	Not specified	ICU and for elective surgery
Braun *(34)*	Not specified	Patients scheduled for coronary angiography
Collinson *(35)*	Not specified	ICU patients
Colucci *(36)*	Not specified	Healthy volunteers
Glas *(37)*	Not specified	Patients undergoing general or trauma surgery
Gomez-Rioja *(38)*	Not specified	Healthy volunteers
Kavsak *(39)*	Not specified	Inpatients from ED, ICU, hematology/oncology, and surgery
Phelan *(40)*	Not specified	Database extract of patient sample values
Thalén *(41)*	Not specified	Healthy volunteers, ICU (8 patients), and cardiovascular clinic
Lima-Oliveira *(28)*	Op1000 (Oppent SpA)	Healthy volunteers
Al-Riyami *(15)*	Sumetzberger	Thalassemia major patients and normal blood donors
Cui *(16)*	Sumetzberger	Healthy blood donors
Koroglu *(17)*	Sumetzberger	58 pancytopenia cases with acute leukemia
Kriegshäuser *(18)*	Sumetzberger	Healthy volunteers
Streichert *(19)*	Sumetzberger	Healthy volunteers
Espinosa *(3)*	Swisslog	Healthy blood donors
Evliyaoglu *(4)*	Swisslog	Inpatients
Kara *(5)*	Swisslog	Unpaired; 49/53 inpatients
Martin *(7)*	Swisslog	Patients with normal hemostasis
Strubi-Vuillaume *(8)*	Swisslog	Patients in a nursery unit
Sylte *(9)*	Swisslog	Outpatients
Lancé *(13)*	Swisslog-ErgoTrans	Elective cardiothoracic surgery
Andersen *(25)*	Tempus	Outpatients
Suchsland *(26)*	Tempus	Healthy volunteers
Fernandes *(10)*	TransLogic CTS-20	Inpatients at 2 different wards
Keshgegian *(11)*	TransLogic CTS-20	Out- and inpatients
Kratz *(12)*	TransLogic (now Swisslog)	Healthy volunteers
Amann *(21)*	Transmatic; Transro	Healthy volunteers
Sari *(14)*	TranspoNet (Swisslog)	Healthy volunteers
Böckel-Frohnhöfer *(23)*	Transro	Departments offering a maximum medical service spectrum
Hübner *(24)*	Transro	Healthy volunteers
Bolliger *(22)*	TR-MC 2000id, Transro	Patients scheduled for coronary artery bypass surgery
Koessler *(6)*	TVS (Swisslog-Telelift)	Healthy volunteers

Discussion

This literature review of published studies on the impact of PTSs on blood samples revealed that despite many investigations, only a few studies were conducted on acutely ill inpatients, and in these studies only selected parameters were investigated, mainly chemistry, hematology, and blood gases. Furthermore, all studies sug-

Table 2. Tubes investigated, the analyses conducted, and the conclusions of the studies.

Study	Tubes used	COAG	ROTEM	PFT	HEMA	BG	CHEM	HI	Conclusion
Sodi *(31)*	Serum, serum gel, lithium heparin, K2EDTA, fluoride EDTA								Compared with serum, with gel plain serum samples are more prone to hemolysis
Böckel-Frohnhöfer *(23)*	Lithium heparin								Significant differences for all analytes
Fernandes *(10)*	Not specified								No significant difference in hemolysis rate
Gomez-Rioja *(38)*	Lithium heparin								A strong linear relation between the TSSAC and hemolysis degree, evidenced by HI and increase in potassium, LD, and ASAT
Kara *(5)*	Without anticoagulant, heparin, K2EDTA or citrate								532-fold higher degree of hemolysis, and differences in potassium, LDH and ALAT
Phelan *(40)*	For potassium (not specified)								No effect
Cui *(16)*	Clot activator, lithium heparin								Significant changes in LDH, while potassium had a slightly rising trend
Kavsak *(39)*	Lithium heparin, pooled samples								Samples from hematology/oncology did not differ, while LDH differed significantly for all wards
Strubi-Vuillaume *(8)*	Lithium heparin								Median bias 18.8%. Reduced with bubble wrapping or using Monovette lithium heparin tubes in aspiration mode
Sylte *(9)*	Gel tubes								The specific sample handling had small but significant effects on results for LD, potassium, glucose, and magnesium
Tiwari *(30)*	Not specified								At high speed, all 3 indices of hemolysis (Hb, K +, and LD) were elevated
Evliyaoglu *(4)*	Heparin, citrate								A positive correlation was observed between distance and hemolysis
Koroglu *(17)*	EDTA and serum gel								Erroneously low PLT counts in patients with leukemia
Suchsland *(26)*	Lithium heparin, K2EDTA, sodium citrate								No effect
Koessler *(6)*	All kinds of tubes								Increase in LD, decrease in leukemia and lymphoma, PT and D-dimer, reduced stimulation of PAC-1 activation; the changes would however not change the clinical interpretation

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Table 2. Tubes investigated, the analyses conducted, and the conclusions of the studies. *(Continued from page XX)*

Study	Tubes used	COAG	ROTEM	PFT	HEMA	BG	CHEM	HI	Conclusion
Andersen *(25)*	Fluoride and citrate, K2EDTA, sodium citrate, lithium heparin	■			■	■	■		Only O_2 saturation, oxyhemoglobin, and pO_2 deviated with clinical significance
Streichert *(19)*	K2EDTA, coagulation, NH4-heparin, serum	■			■	■	■		Speed and the area under the curve exhibited a direct relation to the degree of hemolysis; also, the maximum deviation for a number of components were >20%
Keshgegian *(11)*	All kinds of tubes				■	■	■		No effect
Astles *(33)*	Blood gas syringes					■			Over a wide range, pO_2 tended toward 160 mmHg, which poses a risk of clinical misinterpretation
Collinson *(35)*	Preheparinised syringes					■			Significant alterations in pO_2, no effect on pCO_2 or pH values
Victor Peter *(29)*	Blood gas syringes					■			Clinically unacceptable pO_2 values
Zaman *(32)*	Blood gas syringes					■			If air bubbles cannot be excluded, PTS is not an appropriate transport for pO_2 measurement. No effect on pCO_2 or pH
Al-Riyami *(15)*	K2EDTA				■				No effect
Gossez *(27)*	EDTA				■				No effect
Lima-Oliveira *(28)*	K2EDTA				■				No effect
Sari *(14)*	K2EDTA				■				No effect
Kocak *(20)*	K3EDTA, citrate	■			■				No effect
Kratz *(12)*	K2EDTA, citrate	■			■				No clinically significant effect
Lancé *(13)*	K2EDTA, sodium citrate, citrate + corn trypsin inhibitor		■		■				No effect except for NATEM assays
Martin *(7)*	Sodium citrate (?)		■		■				Thromboelastometry parameters are significantly altered, but in patients with normal hemostasis, the alterations were small and without clinical consequence
Amann *(21)*	Trisodium citrate		■						The higher the acceleration forces, the more ROTEM parameters are influenced
Colucci *(36)*	Trisodium citrate		■						No effect
Espinosa *(3)*	Citrated venous samples		■						Special consideration regarding interpretation of R parameter

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Table 2. Tubes investigated, the analyses conducted, and the conclusions of the studies. *(Continued from page XX)*

Study	Tubes used	COAG	ROTEM	PFT	HEMA	BG	CHEM	HI	Conclusion
Glas *(37)*	Hirudin, citrate								Invalid results in MEA, while only CT in EXTEM was affected
Bolliger *(22)*	Hirudin								Significant influence on Multiplate platelet function testing
Braun *(34)*	Hirudin								Transport of correctly prepared samples does not alter the results of platelet function testing
Hübner *(24)*	Hirudin								Impaired platelet aggregation
Thalén *(41)*	Hirudin								A reduction of area under the curve values of up to a 100% of the average
Kriegshäuser *(18)*[a]	K3EDTA								No effect

COAG, coagulation; ROTEM, rotational thromboelastometry; PFT, platelet function testing; BG, blood gases; HEMA, hematology; CHEM, chemistry/immunochemistry; HI, hemolysis index.
[a] This study included none of the tests mentioned, but only free DNA concentration in plasma from whole blood samples.

gested that it is mandatory to conduct a local investigation of the impact of transportation on blood samples because important parameters such as acceleration vector sums and peak g-force largely are determined by the specific PTS installation.

PTS TESTED

The retrieved studies used several different transportation systems, with 28 using a "regular" tube transportation system (e.g., Swisslog). Nine studies did not specify the PTS used, but an additional 2 studies investigated the Tempus system. The latter is a newly developed system, in which blood tubes are transported without any packing or wrapping by high pressure through a "hose" with a 25-mm diameter. This facilitates an easier handling process at both ends of the PTS, as the tubes can be sent immediately one by one and also are handled immediately when arriving at the lab; most laboratories using this system also have an automated sample receiving unit that places the tube directly into an automated tube track (e.g., Abbott, Roche, or Siemens) that transports the tube directly to the centrifuge and/or to the relevant analysis instrument. This approach decreases the handling processes and any related preanalytical issues, but also increases the number of PTS lines necessary, as every line is unidirectional and only transports blood tubes from A to B (from a ward to the lab), and *not* in the other direction, nor to any other destination. The need for a firm quality assessment protocol of the PTS therefore seems even more important with this system.

STUDY POPULATIONS

As shown in Table 1, only 12 studies were conducted on inpatients, mainly in the ICU.

The remaining studies included healthy persons (16 studies), outpatients (3 studies), highly specialized patient cohorts (7 studies), or were based on data extraction (1 study). In general, it is well known that many blood components, particularly erythrocytes, are more stable in blood from healthy persons, and investigation of the PTS must therefore be conducted on blood from patients, especially vulnerable populations such as cancer patients. Perhaps the patient population should have been an inclusion criterion for the literature review, but we chose to include all studies available to retrieve all relevant information. Altogether, studies on inpatients concluded that the use of a PTS resulted in only minor differences, and the clinical impact was described as minor or nonrelevant. However, it is important to be aware of the large differences in the studies retrieved regarding the number and types of analyses investigated, the population size, and especially the PTS used. Therefore, despite the fact that 23 studies were conducted on inpatients, larger studies are warranted. As a minimum, a local study must be carried out as stated earlier.

AFFECTED PARAMETERS

The retrieved studies included many different analyses, but as previously described only a few studies were on coagulation or platelet function. These parameters are generally urgent and demand a short turnaround time.

For platelets, it has been shown that several preanalytical conditions, e.g., centrifugation, can significantly alter platelet function *(42)*, and platelets could very well be affected by PTS in a similar manner. Also, blood gas testing showed discordant results, reinforcing why a point-of-care test might be preferred for these analyses. Thus, although short turnaround time indeed was achieved with PTS, the discordant study findings strongly advocate for a test of the local PTS to ensure that the specimen transportation modality does not alter the test results.

Since the termination date of our literature search, several studies have emerged on this issue, primarily focusing on coagulation and hematology parameters. This rapid emergence of new information emphasizes the tremendous interest in this area and also the need for standardized quality assessment tools to ease the implementation and use of PTS on every laboratory.

RECOMMENDATIONS

The physical stress induced by the PTS has been found to be closely related to the acceleration, deceleration, length of exposure, and the thermal environment for the specific PTS, but the impact of these variables on samples is difficult to predict theoretically *(19)*. It is therefore necessary to validate the local PTS before transportation of blood samples *(13, 30, 31, 36)*. As a consequence, laboratories using PTS must measure the actual forces in the existing system, e.g., by G-loggers: As suggested by Streichert et al. *(19)*, logging of g-forces during transport nicely depicts the acceleration profile, which is a combination of the maximum g-force measured, the vector sum of acceleration forces, and the transportation distances involved in a given installation. Such loggings can be visualized as a graph, in which the area under the curve has been shown to give a representative, reproducible measurement of the impact of the entire transportation process. Of importance, acceleration vector sums up to 15*g* have been found *not* to increase hemolysis and could perhaps be considered a quality target *(19)*. In this relation, the testing of samples from particularly vulnerable populations such as cancer patients is of the utmost importance. Furthermore, laboratories must also calculate or predict g-forces in future PTS installations by using computer modeling. Owing to the increasing use of PTS, a harmonized, international recommendation on this area is needed as well as a well-defined continuous quality assessment protocol, e.g., using G-loggers.

Conclusion

This literature review could not provide evidence for the safety of using PTSs for blood sample transportation owing to a high degree of heterogeneity observed between the retrieved studies. Surprisingly few studies were conducted on acutely ill inpatients, and further studies are therefore warranted on this patient category. Local investigation of the PTS is mandatory, and for this a harmonized recommendation is needed to ensure a more well-defined validation system of this preanalytical component.

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