Thrombosis Research 228 (2023) 64–71

Contents lists available at ScienceDirect

Thrombosis Research

journal homepage: www.elsevier.com/locate/thromres

Full Length Article

The international normalised ratio to monitor coagulation factor production during normothermic machine perfusion of human donor livers

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ARTICLE INFO

Keywords:
Normothermic machine perfusion
Liver transplantation
Coagulation factors
Hemostasis
International Normalized Ratio
Viability testing

ABSTRACT

Background: Normothermic machine perfusion (NMP) of donor livers allows for new diagnostic and therapeutic strategies. As the liver produces most of the haemostatic proteins, coagulation assays such as the International Normalised Ratio (INR) performed in perfusate may be useful to assess hepatocellular function of donor livers undergoing NMP. However, high concentrations of heparin and low levels of fibrinogen may affect coagulation assays.

Methods: Thirty donor livers that underwent NMP were retrospectively included in this study, of which 18 were subsequently transplanted. We measured INRs in perfusate in presence or absence of exogenously added fibrinogen and/or polybrene. Additionally, we prospectively included 14 donor livers that underwent NMP (of which 11 were transplanted) and measured INR using both a laboratory coagulation analyser and a point-of-care device.

Results: In untreated perfusate samples, the INR was above the detection limit in all donor livers. Addition of both fibrinogen and polybrene was required for adequate INR assessment. INRs decreased over time and detectable perfusate INR values were found in 17/18 donor livers at the end of NMP. INR results were similar between the coagulation analyser and the point-of-care device, but did not correlate with established hepatocellular viability criteria.

Conclusions: Most of the donor livers that were transplanted showed a detectable perfusate INR at the end of NMP, but samples require processing to allow for INR measurements using laboratory coagulation analysers. Point-of-care devices bypass this need for processing. The INR does not correlate with established viability criteria and might therefore have additional predictive value.

1. Introduction

The increase in demand of donor livers requires new strategies regarding organ selection, procurement, and treatment. Whereas explanted organs were initially preserved and transported using static cold storage, novel procedures such as *ex situ* normothermic machine perfusion (NMP) of the liver allow for assessment and resuscitation of donor livers that initially would have been discarded due to "poor" quality (*e.g.*, donation after circulatory death donor livers) [1]. The development of NMP as a method to preserve explanted livers has led to ground-breaking changes in transplantation medicine. Various studies by our and other groups have shown that NMP is safe and might even lead to improved outcome compared to static cold storage [2–6]. As the livers are metabolically active during NMP, this preservation method allows for new diagnostic and therapeutic strategies, such as viability testing [7–9] and therapeutic intervention [10]. Pioneering studies

Abbreviations: ACA, automated coagulation analyser; INR, international normalised ratio; NMP, normothermic machine perfusion; Pb, polybrene; POCD, point-of-care device.

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https://doi.org/10.1016/j.thromres.2023.05.025
Received 15 March 2023; Received in revised form 2 May 2023; Accepted 26 May 2023
Available online 1 June 2023

additionally suggest that explanted livers could potentially be preserved for prolonged periods of time, up to days [11,12], which would provide additional time for therapeutic intervention [13].

A key requirement for acceptance of NMP-perfused donor livers is that they meet viability criteria that reflect graft function. As there is currently no broadly accepted definition of graft viability – with no validated set of viability criteria – protocols concerning viability measurement vary among transplantation centres [9]. Although hepatocellular function remains the main focus of viability testing in the majority of clinical machine perfusion studies to date, increasing attention is also given to additional assessment of cholangiocellular function [14]. Cholangiocellular markers such as bile composition (including bile pH, bicarbonate and glucose levels), are indeed associated with the risk of cholangiopathy after liver transplantation [4,15], and specifically the ratio between bile and perfusate markers might be predictive of cholangiocellular function [16]. Various criteria can be used to assess hepatocellular function, such as lactate metabolism, bile production, haemodynamic stability, glucose metabolism, acid-base balance, and perfusate levels of albumin, urea, and transaminases [9].

An additional important function of the liver is protein synthesis. Many proteins involved in the haemostatic system are synthesized by hepatocytes. We have previously shown that the liver releases relevant amounts of haemostatic factors during NMP [17], presumably by active synthesis. Already after 1 to 2 h of NMP, detectable levels of functional haemostatic factors were present in the perfusate [17]. Studies by other groups have demonstrated that the International Normalised Ratio (INR) measured using a point-of-care device becomes detectable in perfusate samples already after 4 h of NMP [18]. The INR may be specifically interesting as a viability marker, as this measurement can be performed relatively quickly in the diagnostic laboratory or even as a point-of-care test, rather than the extensive measurement of haemostatic proteins using enzyme-linked immunosorbent assays or functional tests. However, most NMP protocols use heparinised circuits with supratherapeutic concentrations of unfractionated heparin, which are known to interfere with INR measurements [19]. Although point-of-care INR devices utilize thrombin generation as an endpoint and contain a heparin-neutralising substance in the reagent [20,21], the exact components of these test strips are confidential and heparin sensitivity studies have only been reported at a maximum dose of unfractionated heparin of 2 U/mL. Little is thus known about the applicability of these devices in *ex situ* machine perfusion of donor organs, in which heparin concentrations may be substantially higher. Additionally, we have previously shown that fibrinogen perfusate levels are very low in perfusate during liver NMP [17]. Since routine diagnostic tests in plasma have clot formation as the endpoint of the test, low fibrinogen levels may complicate INR measurements. The aim of this study was therefore to assess whether INR measurements are possible in perfusate samples of NMP donor livers, and whether this marker may be a potential viability marker for hepatocellular function during NMP.

2. Methods

2.1. Study samples

In 2019, the DHOPE-COR-NMP protocol [3,16,22] has been implemented as standard procedure for initially discarded human livers at the University Medical Center Groningen. The study protocol was approved by the Medical Ethical Committee and registered in the Netherlands Trial Register (NTR5972), and the study was conducted in accordance with the Declaration of Helsinki. Donor livers were included in the DHOPE-COR-NMP protocol if patients provided written informed consent and if the donor liver was rejected for immediate transplantation by all three transplantation centres in the Netherlands. Details on the donor liver procurement, machine perfusion and hepatobiliary viability assessment have been described previously by our group [3]. Specific criteria used to determine viability at 2.5 h of NMP in our centre are depicted in Supplementary Table S1. Details of the perfusion solution are shown in Supplementary Table S2. Of note, the perfusion fluid at the start of the controlled oxygenated rewarming contains 10.000 IU of unfractionated heparin in a total volume of 2065 mL, and additional doses of 1.000 IU were added to the circuit every hour until end of NMP.

Perfusate samples of NMP donor livers were included retrospectively from January 1, 2019 to April 8, 2021, and prospectively from April 8, 2021 to May 25, 2022. Retrospectively included samples were collected in vacuum tubes containing 3.2 % sodium citrate, with a perfusate to anticoagulant ratio of 9:1. Prospectively included samples were collected in either 3.2 % sodium citrate tubes or a tube without any anticoagulant. A first sample was taken at the time of hepatobiliary viability assessment 2.5 h after start of NMP. If the liver did not meet viability criteria as previously described at 2.5 h of NMP [3,16], the NMP procedure was terminated, and the liver was secondarily discarded. If the liver met viability criteria and was thus accepted for transplantation, NMP of the liver proceeded until hepatectomy of the recipient was completed. Additional perfusate samples were collected 3 h, 5 h, 6 h and 7 h after the start of NMP in retrospectively included donor livers, and at the end of NMP in prospectively included donor livers (Supplementary Fig. 1).

To assess the effect of heparin on our assays, we included blood samples of 3 healthy volunteers collected in vacuum tubes containing either 3.2 % sodium citrate (at a blood-to-anticoagulant ratio of 9:1) or unfractionated heparin (final concentrations 5 U/mL and 10 U/mL in plasma). Also, we used human fibrinogen-deficient plasma (Nodia, Amsterdam, the Netherlands) and added various amounts of fibrinogen (final concentrations 0.125 g/L, 0.25 g/L, 0.5 g/L, 1 g/L, 2 g/L and 4 g/L) to assess the effect of fibrinogen deficiency on our assays. (Supplementary Fig. 1).

2.2. Coagulation assays

The INR of all included samples was assessed using the STA Compact Max3 analyser with reagents and protocols from the manufacturer (Stago, Breda, the Netherlands). In perfusate samples taken during DHOPE-COR-NMP, the INR was measured either without any addition, after addition of 380 μg/mL polybrene (which neutralises the anticoagulant effects of heparin), after addition of 1 g/L fibrinogen, or after addition of both polybrene and fibrinogen. The INR of prospectively collected samples was also assessed using the point-of-care test CoaguChek Pro II (Roche Diagnostics, Mannheim, Germany). In samples taken from healthy volunteers, the INR was measured using both the STA Compact Max3 analyser (with or without addition of polybrene) and the CoaguChek Pro II. After addition of various amounts of fibrinogen, the INR of the fibrinogen deficient plasma was measured using the STA Compact Max3 analyser.

Fibrinogen levels were measured on a STA Compact Max3 analyser with reagents and protocols from the manufacturer (Stago, Breda, the Netherlands). Anti-Xa activity was measured on STA Compact Max3 analyser using Heparin LRT (Hyphen Biomed, Amsterdam, The Netherlands). As the low antithrombin levels in these perfusates could underestimate anti-Xa activity, we measured anti-Xa activity in the presence of 1 Plasma Equivalent Unit of antithrombin (Hyphen Biomed, Amsterdam, the Netherlands) added to the test sample.

2.3. Statistical analyses

Statistical analyses were performed using GraphPad Prism v9 and SPSS Statistics 28 (IBM). Data are expressed as means (with standard deviation), medians (with interquartile ranges (IQR)) or numbers (with percentages) as appropriate. Continuous variables were analysed using the Mann-Whitney *U* test, categorical variables using the Chi-squared test. Spearman's correlation coefficient was used to assess the association between continuous variables. Statistical significance was established at $p < 0.05$.

3. Results

3.1. Levels of fibrinogen and heparin affect INR measurements in human plasma

We added various concentrations of fibrinogen to fibrinogen-deficient human plasma, and measured INR on an automated coagulation analyser (Fig. 1a). Compared to INR values measured in the presence of 4 g/L of fibrinogen, INRs were substantially prolonged at fibrinogen levels of 0.5 g/L or lower.

Next, we assessed the effect of unfractionated heparin on the measurement of INR in plasma of 3 healthy volunteers (Fig. 1b). After addition of 5 U/mL of heparin, INRs assessed with an automated coagulation analyser increased from 1.00 (IQR 1.00–1.00) to 2.20 (IQR 1.40–2.53). After addition of 10 U/mL of heparin, the INR was above the detection limit of 12 in 2/3 samples, and 11.1 in 1/3 samples. Addition of 380 μg/mL of polybrene restored INRs of all samples to <1.5. When whole blood of the same volunteers was tested with a point-of-care analyser, addition of heparin did not increase the INR.

3.2. INR measurements using routine laboratory methodology are not possible in unmodified perfusate samples

Retrospectively collected, heparinised perfusate samples of 30 initially declined donor livers donated after circulatory death were included. Of these donor livers, 18 (60 %) were subsequently transplanted after meeting viability criteria. Of the 12 donor livers that did not meet viability criteria, one did not meet the perfusate pH criterium, ten did not meet the bile minus perfusate pH criterium, and ten did not meet the bile minus perfusate bicarbonate criterium. Details on donor livers and analyses of perfusate samples are shown in Table 1. In total, we were able to analyse samples of 18 out of 18 subsequently transplanted donor livers at time of viability testing (2.5 h of NMP), of 16 donor livers after 3 h of NMP, of 15 donor livers after 5 h of NMP, of 14 donor livers after 6 h of NMP, and of 7 donor livers after 7 h of NMP. Fibrinogen levels were below the detection limit of 0.23 g/L in most samples (of 10 out of 12 discarded livers and 16 out of 18 transplanted livers) at the time of viability testing, and levels were similar in discarded and transplanted donor livers at this time point (Fig. 2a). Fibrinogen levels increased over time, but were still <1 g/L in samples taken after 7 h of NMP. Anti-Xa levels at the time of viability testing were similar in transplanted and discarded livers (Fig. 2b).

We performed INR measurements of perfusate samples on a routine diagnostic coagulation analyser. In all of the perfusate samples studied INR values were above the detection limit (of 12) (Fig. 3a). To assess the role of fibrinogen deficiency in the inability to measure an INR in these samples, we repeated INR measurements after addition of 1 g/L of fibrinogen. After addition of fibrinogen, we were able to measure the INR in samples of one donor liver that has been transplanted after 3 h of NMP – however, in the remainder of samples the INR remained above the detection limit during the course of the entire NMP procedure (Fig. 3b). To assess the role of the high heparin concentrations in the perfusate in the inability to measure an INR in these samples, we tested the INR in the presence of 380 μg/mL polybrene, which neutralises the anticoagulant effects of heparin. After addition of polybrene, we were able to measure an INR at the end of NMP in a total of 15 out of 18 donor livers that have been transplanted (Fig. 3c). Addition of both 1 g/L of fibrinogen and 380 μg/mL of polybrene resulted in a measurable INR at the end of NMP in 17 out of 18 of donor livers that have been transplanted, with a measurable INR at the time of viability testing in 8 out of 18 livers (Fig. 3d). In donor livers that were discarded after 2.5 h of NMP, none had a measurable INR at the time of viability testing. The percentage of livers with a detectable INR at the time of viability testing was significantly higher in the livers that were eventually transplanted compared to those that were discarded (p = 0.01). INR values decreased gradually over the course of the NMP procedure (Fig. 4).

Table 1
Donor characteristics of retrospectively included donor livers.

	Transplanted (n = 18)	Not transplanted (n = 12)	p-Value
Age (years)	66 [59–68]	68 [55–74]	0.361
Body mass index (kg/m^2)	27 [25–30]	25 [24–27]	0.114
Gender			
Female	4 (22 %)	8 (67 %)	**0.015**
Male	14 (78 %)	4 (33 %)	
Cause of death			
Cerebrovascular attack	8 (44 %)	7 (58 %)	0.774
Anoxia	6 (33 %)	2 (17 %)	
Trauma	3 (17 %)	2 (17 %)	
Other	1 (6 %)	1 (8 %)	
Reason for primary rejection			
Age > 60 years	14 (78 %)	9 (75 %)	0.227
Body mass index > 35 kg/m^2	2 (11 %)	0	
Traumatic laesion liver parenchyma	2 (11 %)	0	
Abnormal liver anatomy	0	2 (17 %)	
Functional donor warm ischaemia time > 30 min	0	1 (8 %)	
Functional donor warm ischemia time (min)	28 [25–32]	32 [28–35]	0.120
Static cold ischemia time (hours)	4.53 [3.98–4.86]	4.64 [4.48–5.28]	0.156
Total duration of normothermic machine perfusion			
2.5 h	0	12 (100 %)	**<0.001**
3 h	3 (17 %)	0	
5 h	0	0	
6 h	8 (44 %)	0	
7 h	7 (39 %)	0	

Continuous data are presented as median [IQR], categorical data as number (percentage). P-values in bold indicate p-values <0.05.

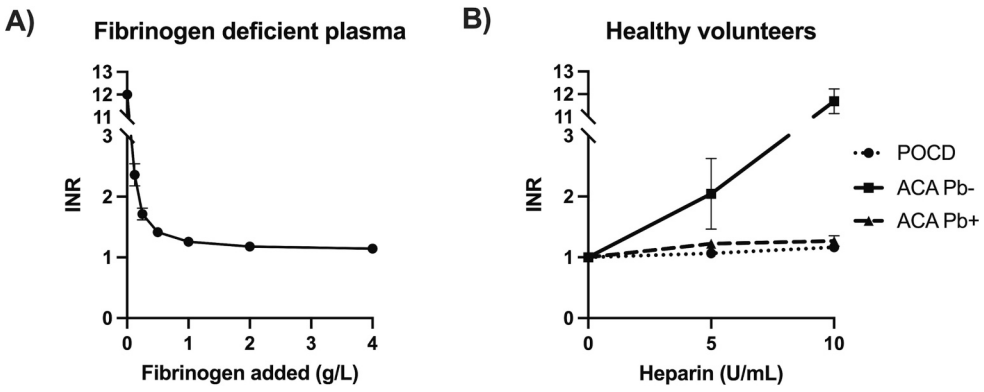

Fig. 1. The International Normalised Ratio (INR) in A) fibrinogen deficient human plasma after addition of various concentrations of fibrinogen. Shown are mean values of 3 independent experiments, error bars indicate standard deviations, and B) blood samples of three healthy volunteers after addition of 5 or 10 U/mL of unfractionated heparin (final concentration in plasma). Whole blood samples were measured using the point-of-care device (POCD), and plasma samples were analysed using an automated coagulation analyser (ACA) with or without addition of 380 μg/mL of polybrene (Pb). Shown are means, error bars indicate standard deviations.

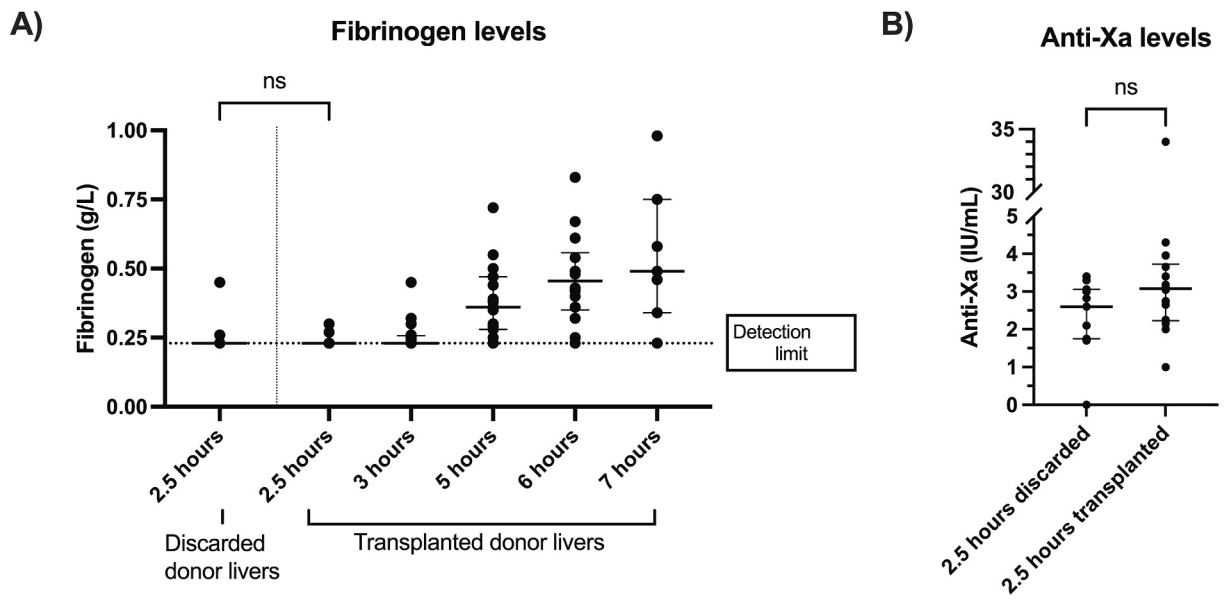

Fig. 2. Levels of A) fibrinogen and B) anti-Xa in perfusates of normothermic machine perfused donor livers. Horizontal lines indicate medians, error bars indicate interquartile ranges.

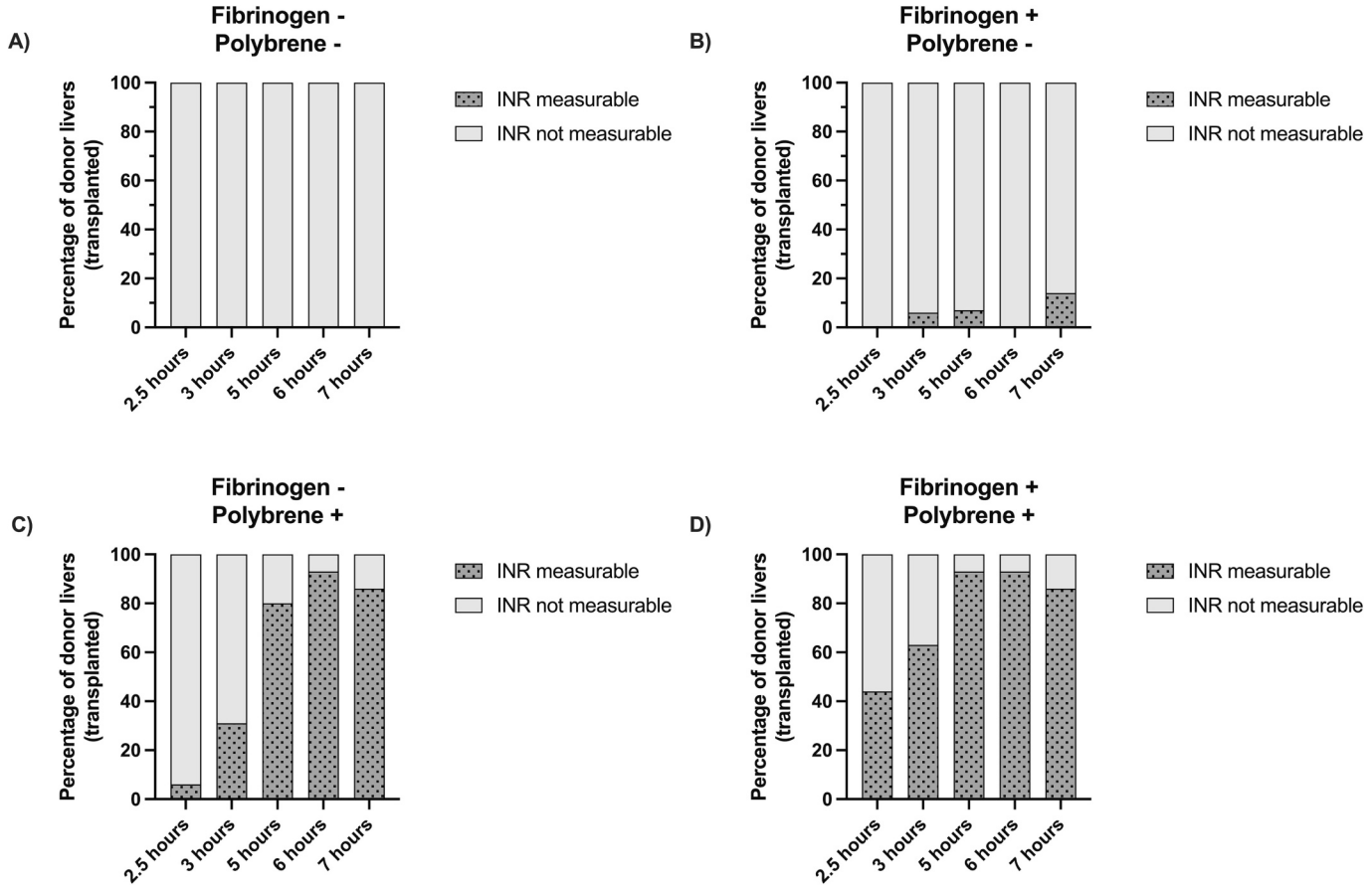

Fig. 3. Perfusate samples taken during the course of normothermic machine perfusion were assayed for International Normalised Ratio (INR) using an automated coagulation analyser, A) without any additions, B) after addition of 1 g/L of fibrinogen, C) after addition of 380 μg/mL of polybrene, or D) after addition of both 1 g/L of fibrinogen and 380 μg/mL of polybrene. Shown are the percentage of transplanted donor livers with a detectable perfusate INR at the various time points indicated.

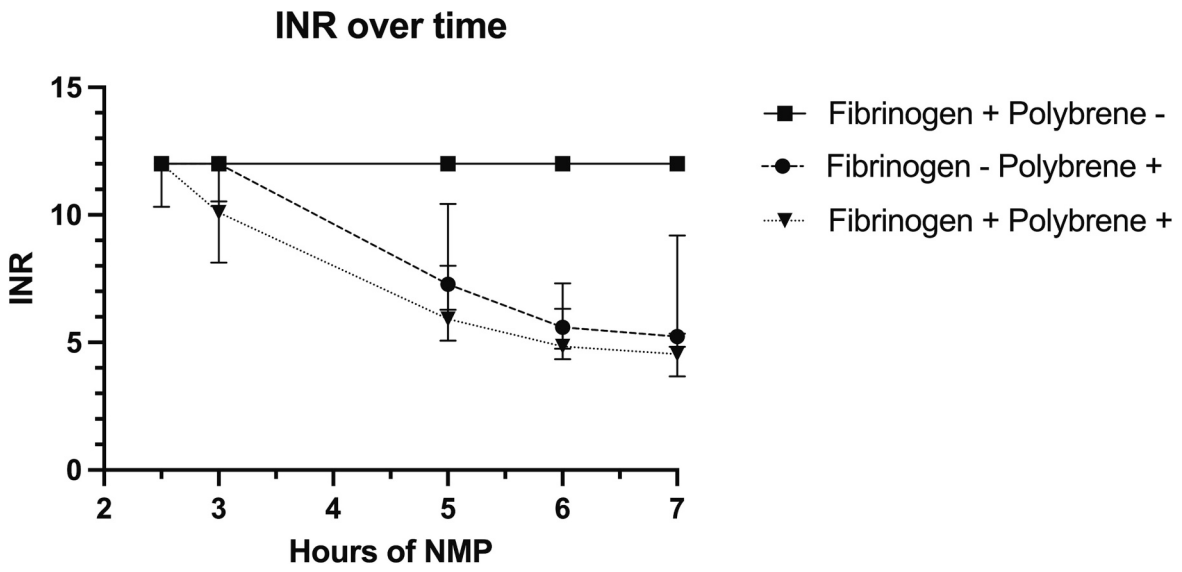

Fig. 4. Perfusate samples taken during the course of normothermic machine perfusion (NMP) were assayed for International Normalised Ratio (INR) using an automated coagulation analyser after addition of 380 μg/mL polybrene, after addition of 1 g/L fibrinogen, or after addition of both polybrene and fibrinogen. Shown are the INR results at the various time points, error lines indicate interquartile range.

3.3. Unmodified perfusate samples give INR results on a point-of-care analyser that are similar to those obtained with the modified INR on a coagulation analyser

Prospectively collected perfusate samples of 14 initially declined donor livers donated after circulatory death were included to assess the ability of the point-of-care device in measuring INR in an NMP setting. Of these donor livers, 11 (76 %) were subsequently transplanted after meeting viability criteria. Of the three livers that did not meet the viability criteria, three did not meet the bile minus perfusate pH criterium, two did not meet the bile minus perfusate bicarbonate criterium, and one did not meet the bile minus perfusate glucose criterium. Details on donor livers and analyses of perfusate samples are shown in Table 2. At the time of viability testing, none of the samples tested using the point-of-care device were below the INR detection limit of 8. Seven of the 14 livers - 5 out of 11 transplanted livers, 2 out of 3 discarded livers - had a detectable INR on the coagulation analyser when polybrene and fibrinogen were added (INRs ranging from 5.4 to 10.6) at the time of viability testing, but the detection limit of the coagulation analyser is substantially higher (12 rather than 8). In 9 out of 11 transplanted donor livers INRs were detected by the point-of-care device at the end of the NMP procedure (after 6 h in 1 liver, 7 h in 8 livers, 8 h in 1 liver, and 9 h in 1 liver). The INR as measured on a coagulation analyser (with addition of either polybrene only or polybrene and fibrinogen) correlated well with the INR as measured by the point-of-care device in these samples (Fig. 5).

3.4. No correlation between INR and other hepatocellular viability criteria

To analyse the correlation between INR and other viability criteria used in clinical settings, we combined data of both retrospectively and prospectively included donor livers. At the time of viability testing, perfusate samples of donor livers with INRs above the detection limit of 12 (after addition of fibrinogen and polybrene) were excluded from analyses, resulting in a total of 8 out of 30 retrospectively and 8 out of 14 prospectively included donor livers. INR at viability testing did not correlate with perfusate lactate or perfusate pH (Fig. 6a-b). At the end of NMP, perfusate samples of donor livers with INR above the detection limit of 12 (after addition of fibrinogen and polybrene) were excluded from analyses, resulting in a total of 17 out of 18 retrospectively and all 11 prospectively included donor livers that were subsequently transplanted. Again, INR at the end of NMP did not correlate with perfusate lactate or perfusate pH (Fig. 6c-d).

Table 2
Donor characteristics of prospectively included donor livers.

	Transplanted (n = 11)	Not transplanted (n = 3)	p-Value
Age (years)	63 [61–68]	60 [53–68]	0.390
Body mass index (kg/m^2)	26 [25–34]	26 [24–27]	0.433
Gender			
Female	7 (64 %)	0 (0 %)	0.217
Male	4 (36 %)	3 (100 %)	
Cause of death			
Cerebrovascular attack	1 (9 %)	2 (67 %)	0.184
Anoxia	7 (64 %)	1 (33 %)	
Trauma	2 (18 %)	0 (0 %)	
Other	1 (9 %)	0 (0 %)	
Reason for primary rejection			
Age > 60 years	10 (91 %)	2 (67 %)	0.129
Body mass index > 35 kg/m^2	1 (9 %)	0	
Functional donor warm ischaemia time > 30 min	0	1 (33 %)	
Functional donor warm ischemia time (min)	32 [29–63]	28 [14–55]	0.311
Static cold ischemia time (min)	4.20 [3.11–4.93]	3.23 [2.82–3.93]	0.237
Total duration of normothermic machine perfusion			
2.5 h	0	3 (100 %)	**<0.001**
3 h	0	0	
5 h	0	0	
6 h	1 (9 %)	0	
7 h	10 (91 %)	0	

Continuous data are presented as median [IQR], categorical data as number (percentage). P-values in bold indicate p-values <0.05.

4. Discussion

Here, we provide proof of concept that it is possible to measure INR in the perfusate of livers that undergo NMP using both a point-of-care analyser and routine diagnostic methodology. However, measuring INR using a routine diagnostic coagulation analyser requires additional

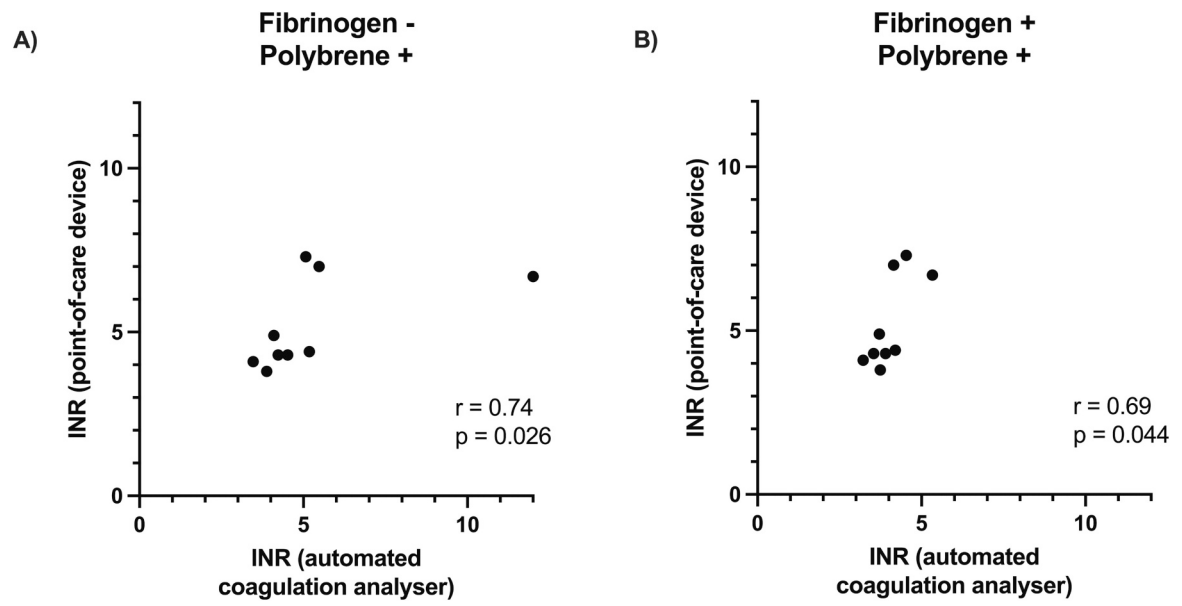

Fig. 5. Correlation between the International Normalised Ratio (INR) at the end of the normothermic machine perfusion procedure as measured by A) an automated coagulation analyser (with the addition of either polybrene only or polybrene and fibrinogen) and B) a point-of-care device, with Spearman's correlation coefficients.

processing of the perfusate samples to compensate for the effect of low levels of fibrinogen and high levels of heparin. To the best of our knowledge, we are the first to provide a validated approach to measure INR values in NMP perfusates using routine diagnostic methods. An alternative for measuring INR using routine laboratory assays is a point-of-care device such as the CoaguChek, which is insensitive to the high levels of heparin present in these perfusate samples due to the presence of a heparin-neutralising agent in the reagent, and is insensitive for low fibrinogen levels. In accordance with the study by Banan et al. [18], we demonstrated that the INR as measured by an automated coagulation analyser gradually decreases over time during the NMP procedure. Importantly, we have validated the approach by Banan et al., by demonstrating that the CoaguCheck indeed is insensitive to the high heparin and low fibrinogen levels present in clinical NMP samples.

In preservation of donor livers using NMP, the INR might have value as a viability marker, as protein synthesis is an important hepatocellular function that is not tested in current viability testing protocols. Even though the INR is not yet measurable in the majority of livers at the time of viability testing (2.5 h in our centre), we were able to measure an INR after 5 h of NMP in all but one donor livers that were subsequently transplanted. The INR might therefore be more suitable as a viability marker in settings of prolonged NMP preservation of donor livers, or in settings in which the donor liver is immediately connected to a NMP circuit without prior cold preservation. Firstly, with the current rate of innovation and progress in the procurement of donor livers, NMP could be used in the future to apply regenerative therapeutic approaches [13]. The INR could be used, for example, to monitor hepatocellular function during experiments on novel therapies, such as defattening strategies or RNA interference, in settings of prolonged preservation using NMP. Secondly, there is increasing interest in the possibility to perform ischaemia-free liver transplantation, c.q. transplantation with minimal to no cold or warm ischaemia time [23]. Pioneer studies using porcine livers by Banan et al. show that in contrast to a setting in which the liver has been cooled down and rewarmed before the start of NMP (as is the case in our current study), the INR is already measurable at the start of NMP in settings without cooling and rewarming [24]. Specifically in the setting of immediate NMP or "ischaemia-free" NMP, the INR may thus potentially have value as an early viability criterium. However, further research on the application of INR in this setting should be performed prior to clinical implementation.

Although previous studies have shown that individual coagulation factors, such as factor V, may be detectable even in the first hours of NMP [17] and may have predictive value at 48 h of NMP [11], the INR has the advantage that measurement can be performed relatively quickly in the diagnostic laboratory after addition of fibrinogen and polybrene. Point-of-care devices are insensitive to the high levels of unfractionated heparin and low levels of fibrinogen in the perfusate samples, which allows for even more rapid INR measurements without the requirement for addition of polybrene and fibrinogen.

Despite the limitations of a small sample size and a relatively short perfusion period, this is to our knowledge the first study that explores the methodology behind measuring INR during NMP of donor livers. Previous work by Banan [18] has shown that it is possible to measure INR during NMP using a point-of-care device. The current study, however, is the first to demonstrate that the INR can also be measured using routine coagulation analysers, and that results of these two methodologies correlate well. In the majority of hospitals that use NMP in a clinical setting, hepatocellular function is defined and scored by production of bile, metabolism of lactate and glucose and management of pH-levels in perfusate [9]. However, none of these viability criteria reflects the hepatocellular ability to synthesise plasma proteins. Interestingly, our study shows that when we are able to detect an INR after 2.5 h of NMP, it does not correlate with other hepatocellular viability criteria at this same time point. Similarly, there was no correlation between INR and other hepatocellular viability criteria at the end of NMP. This may suggest that the synthetic function of the liver as measured by haemostatic proteins is an independent marker of hepatocellular function, which is not captured by the currently used viability markers. However, due to the small sample size, we were unfortunately not able to assess associations between INRs as measured during NMP and outcome measures such as early post-transplant graft function or other graft-related complications. Moreover, inherent to the nature of our clinical NMP protocol, we do not know what would have been the postoperative outcome of the livers that were secondarily discarded after NMP testing. Future research is also required to investigate the predictive value of INR as a viability marker in (prolonged) NMP procedures.

In conclusion, we were able to measure INR perfusate samples in the majority of NMP donor livers. The perfusate samples, however, need processing before routine laboratory assays can be performed. Point-of-care devices for INR measurement bypass this need for processing and

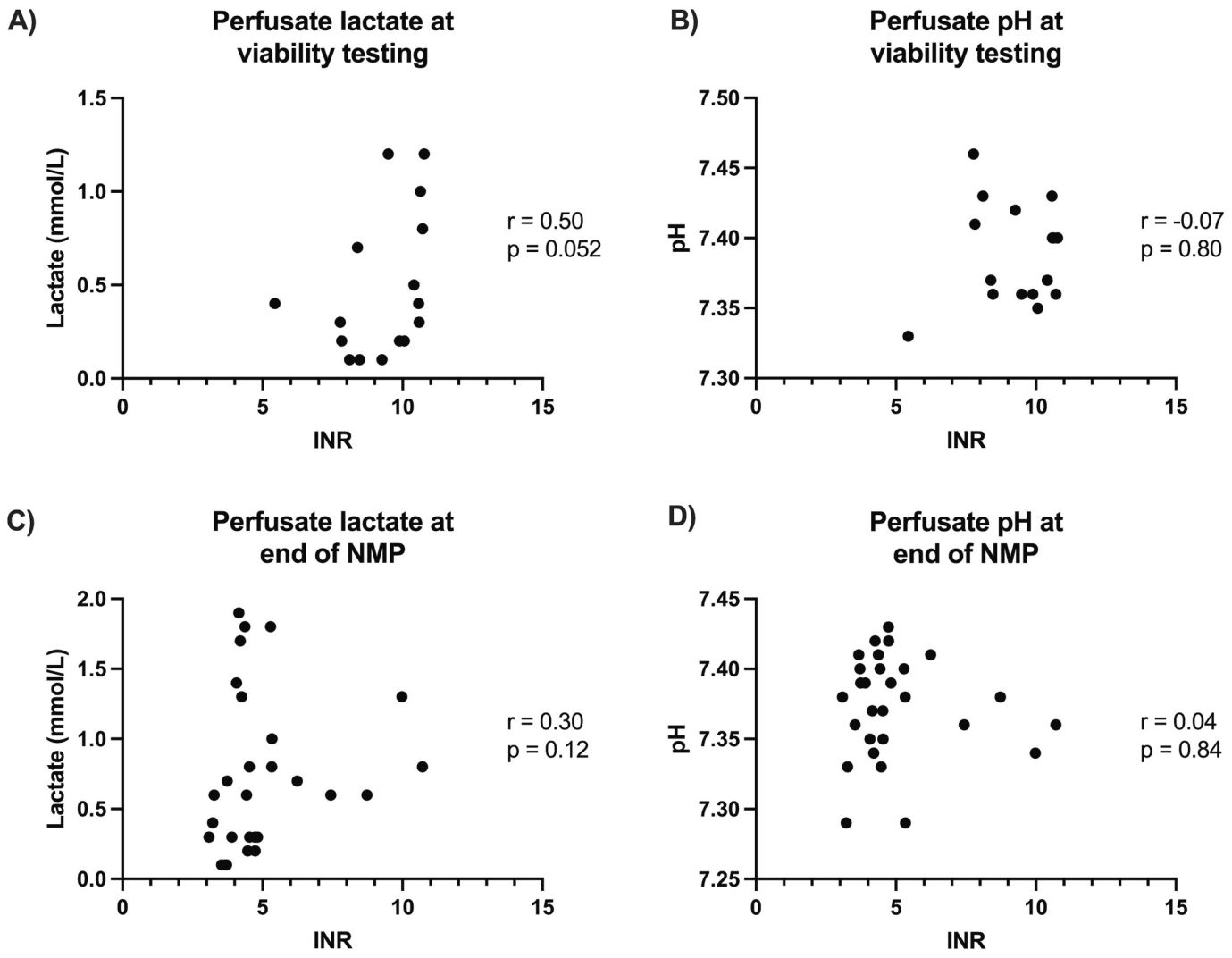

Fig. 6. Correlation between perfusate International Normalised Ratio (INR) as measured by a fibrinogen and polybrene modified test on an automated coagulation analyser and A) perfusate lactate at viability testing (2.5 h of normothermic machine perfusion (NMP)), B) perfusate pH at viability testing, C) perfusate lactate at end of NMP, and D) perfusate pH at end of NMP, with Spearman's correlation coefficients.

might thus be an alternative to routine laboratory assays. After 5 h of NMP, we were able to measure an INR in NMP perfusate samples of all but one donor livers that were accepted for transplantation. Interestingly, the INR did not correlate with other viability criteria at the time of viability testing (2.5 h of NMP) or at the end of NMP, suggesting that INR measurement may therefore have additional value as a viability criterium (especially during prolonged periods of NMP).

Supplementary data to this article can be found online at https://doi.org/10.1016/j.thromres.2023.05.025.

Financial statement

VM reports a VENI research grant by the Dutch Research Council (NWO; grant #09150161810030), a Research grant from the Dutch Ministry of Economic Affairs (Health~Holland Public Private Partnership grant #PPP-2019-024), and a Research grant from the Dutch Society for Gastroenterology (NVGE #01-2021), all outside the submitted work.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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