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Lack of agreement between different observers and methods in the measurement of capillary refill time in healthy volunteers: an observational study

Falta de concordância entre diferentes observadores e métodos na mensuração do tempo de reenchimento capilar em voluntários saudáveis: estudo observacional

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ABSTRACT

Objective: Peripheral perfusion abnormalities are relevant manifestations of shock. Capillary refill time is commonly used for their evaluation. However, the reproducibility of capillary refill time measurements and their correlation with other variables of peripheral perfusion, have not been comprehensively evaluated. Our goal was to determine, in healthy volunteers, the agreement between different methods of capillary refill time quantification and different observers, as well as their correlation with other markers of peripheral perfusion.

Methods: We studied 63 healthy volunteers. Two observers measured capillary refill time by means of two methods, direct view ($CRT_{chronometer}$) and video analysis (CRT_{video}). We also measured perfusion index (PI) derived from pulse plethysmography and finger pad temperature ($T°_{peripheral}$). The agreement between observers and methods was assessed using the Bland and Altman method. Correlations were calculated using Pearson's correlation. A p-value<0.05 was considered significant.

Results: The 95% limits of agreement between the two observers were 1.9 sec for $CRT_{chronometer}$ and 1.7 sec for CRT_{video}. The 95% limits of agreement between $CRT_{chronometer}$ and CRT_{video} were 1.7 sec for observer 1 and 2.3 sec for observer 2. Measurements of $CRT_{chronometer}$ performed by the two observers were correlated with $T°_{peripheral}$. Measurements of CRT_{video} performed by the two observers were correlated with $T°_{peripheral}$ and perfusion index.

Conclusion: In healthy volunteers, measurements of capillary refill time performed by either different observers or different methods showed poor agreement. Nevertheless, capillary refill time still reflected peripheral perfusion as shown by its correlation with objective variables of peripheral perfusion.

Keywords: Shock/diagnosis; Perfusion; Capillaries/physiology

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INTRODUCTION

Alterations in peripheral perfusion are a key finding amongst the clinical manifestations of shock. Not only are clinical signs of poor peripheral perfusion early indicators of hemodynamic instability, but they are also strong predictors of later complications and death.[1,2] Peripheral perfusion can be assessed in several ways, of which capillary refill time (CRT) is one of the most common.

CRT is defined as the time required for a distal capillary bed to regain its color after having received enough pressure to cause blanching. CRT can be

measured with different techniques and is susceptible to factors that can deeply affect the results, such as environmental, skin and core temperatures, age, ambient light conditions, and the duration, amount and site of pressure application.[3] Nevertheless, these issues are rarely considered by physicians.[4]

A further source of uncertainty is the dependency on the observer´s performance. Marked interobserver variability was found when applied to healthy children[5] and newborns,[6] in cardiac surgery,[7] and in pediatric patients with shock.[8] Despite the relevance of CRT for the clinical evaluation of tissue perfusion, its reproducibility remains insufficiently studied in adults. Poor interobserver agreement was reported in adult patients admitted to an emergency department, where CRT was unfortunately estimated without a timing device.[9] Proper quantification with a chronometer may have produced different results.

The goal of this study was to evaluate the reliability of CRT measurement in adult healthy volunteers, as well as its correlation with objective variables of peripheral perfusion. For this purpose, CRT was evaluated by two different observers and by two different methods. Our hypothesis was that CRT has poor reproducibility.

METHODS

We carried out a prospective observational study with healthy volunteers older than 18 years of age. Our study was approved by the Institutional Review Board. Volunteers signed informed consent forms after receiving written and oral information.

All patients were evaluated after 10 minutes of rest while sitting upright in a climate-controlled environment with a temperature of 25º C. CRT was measured by applying firm pressure by means of a slide to the distal phalanx pad of the right fourth finger for at least 5 seconds. First, under direct visualization, a chronometer was used to measure the time from release of pressure to the return of normal color ($CRT_{chronometer}$). This procedure was repeated by a second observer, blind to the previous measurement.

CRT was also quantified by analysis of videos of these measurements (CRT_{video}) taken with a Nikon D3100 digital camera (Nikon Corporation, Tokyo, Japan) positioned on a tripod 20 cm from the finger pad. This procedure was performed by two investigators who were blind to the results acquired by the $CRT_{chronometer}$ technique. The film-editing software iMovie 2009 (Apple Inc., version 8.0.6), which allowed frame-by-frame (30 fps) inspection on a computer screen, was used for the analysis. CRT_{video} was established during direct observation of the video in slow motion mode as the time elapsed between the release of the pressure and the frame in which the observer identified the recovery of basal color.

We also measured heart rate, arterial blood pressure in the left arm by an automatic sphygmomanometer, second finger pad temperature by a skin thermistor ($T°_{peripheral}$), and perfusion index derived from the pulse oximetry signal in the right third finger. The perfusion index is the ratio between the pulsatile and the nonpulsatile component of the light reaching the detector of the pulse oximeter. In presence of peripheral hypoperfusion, the pulsatile component decreases, and because the nonpulsatile component is unchanged, the ratio also decreases.

Statistical analysis

Data were tested for normality by the Kolmogorov-Smirnov test and expressed as the mean±standard deviation (SD). The superior limit of normality was determined as the mean±2 SD. Agreement between different methods and observers for the measurement of CRT was calculated by the method of Bland and Altman. Correlations between CRT and indices of peripheral perfusion were evaluated by Pearson's correlation. Given the lack of data in the literature, the sample size was not calculated, but its adequacy was tested.[10] A p-value<0.05 was considered as significant.

RESULTS

Using the formula for calculating 95% confidence interval ($CI95\%=1.96\sqrt{[3s2/n]}$) with our sample size of 63 for an "s" (SD of the differences between the two observers for the measurement of $CRT_{chronometer}$) of 0.5 sec, our CI was 0.29-0.71 sec, which we found acceptable.[10] This calculation was performed for every comparison and the CI95% were similar: 0.23-0.57 for the SD of the differences between the two observers for the measurement of CRT_{video}, 0.23-0.57 for the SD of the differences between the two methods by Observer 1, and 0.34-0.86 for the SD of the differences between the two methods by Observer 2.

Table 1 shows the characteristics of the studied volunteers. $CRT_{chronometer}$ was similar for both genders (female versus male, 1.3±0.4 versus 1.3±0.5 sec, p=0.92 for observer 1, and 1.4±0.8 versus 1.3±0.5 sec, p=0.45

for observer 2). With CRT_{video}, the results were similar (1.0±0.3 versus 1.2±0.6 sec, p=0.11 for observer 1, and 1.2±0.6 versus 1.2±0.4 sec, p=0.67 for observer 2). Age was not correlated with $CRT_{chronometer}$ (R=0.11, p=0.39 for observer 1, and R=0.17, p=0.17 for observer 2) or CRT_{video} (R=0.17, p=0.16 for observer 1, and R=0.01, p=0.96 for observer 2).

Table 1 - Epidemiologic and physiologic data of healthy volunteers (n=63)

Variables	Results
Age (years)	40±11
Sex, male (n, %)	24 (38)
Heart rate (beats/minute)	73±10
Mean arterial blood pressure (mmHg)	87±10
Chronometric capillary refill time (sec)	
Observer 1	1.3±0.5
Observer 2	1.3±0.7
Video capillary refill time (sec)	
Observer 1	1.2±0.5
Observer 2	1.1±0.5
Chronometric capillary refill time limit of normality (sec)	
Observer 1	2.2
Observer 2	2.7
Video capillary refill time limit of normality (sec)	
Observer 1	2.2
Observer 2	2.0
Peripheral temperature (°C)	31.9±2.2
Perfusion index	4.4±2.7

Results are expressed as number (%) or mean±standard deviation.

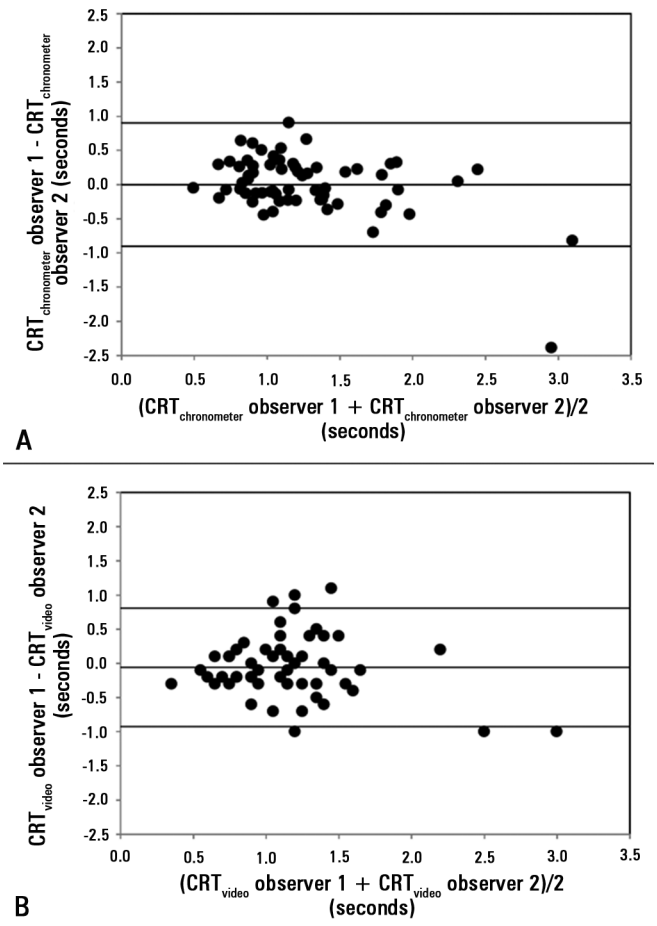

Figure 1 - Bland and Altman analysis for the agreement between measurements of capillary refill time performed by two different observers. Panel A shows capillary refill time measured by a chronometer during the direct visualization ($CRT_{chronometer}$) and Panel B capillary refill time performed by video analysis (CRT_{video}). Horizontal lines represent bias and 95% limits of agreement. CRT - capillary refill time.

With regard to Bland and Altman analysis, bias±precision between observers was 0.0±0.5 sec for $CRT_{chronometer}$ and -0.1±0.4 sec for CRT_{video} (p=0.46) (Figure 1). Bias±precision between CRT_{video} and $CRT_{chronometer}$ was -0.1±0.4 sec for observer 1 and -0.2±0.6 sec for observer 2 (p=0.15) (Figure 2).

The measurements of $CRT_{chronometer}$ and CRT_{video} performed by observer 1 were correlated with $T°_{peripheral}$ and perfusion index, but the correlation between $CRT_{chronometer}$ and perfusion index did not reach statistical significance (Figure 3). Similar correlations were found with the data from observer 2 (Figure 4). $CRT_{chronometer}$ and CRT_{video} also correlated with heart rate (R=-0.27 and -0.38, respectively, p<0.05, for observer 1, and R=-0.31 and -0.31, respectively, p<0.05, for observer 2), but not with mean arterial blood pressure (R=-0.19 and -0.06, respectively, p=not significant (NS), for observer 1, and R=-0.20 and 0.18, respectively, p=NS, for observer 2).

DISCUSSION

The main finding of this study is the lack of reproducibility for CRT. Measurements performed by different observers and different methods exhibited poor agreement. Despite these limitations, CRT still reflected peripheral perfusion as shown by its correlation with objective variables, such as $T°_{peripheral}$ and the perfusion index.

The measurement of CRT is a common approach for the evaluation of peripheral perfusion. It was first described in 1947 as a means of grading the severity of shock.[11] Thereafter, it was included in the trauma score

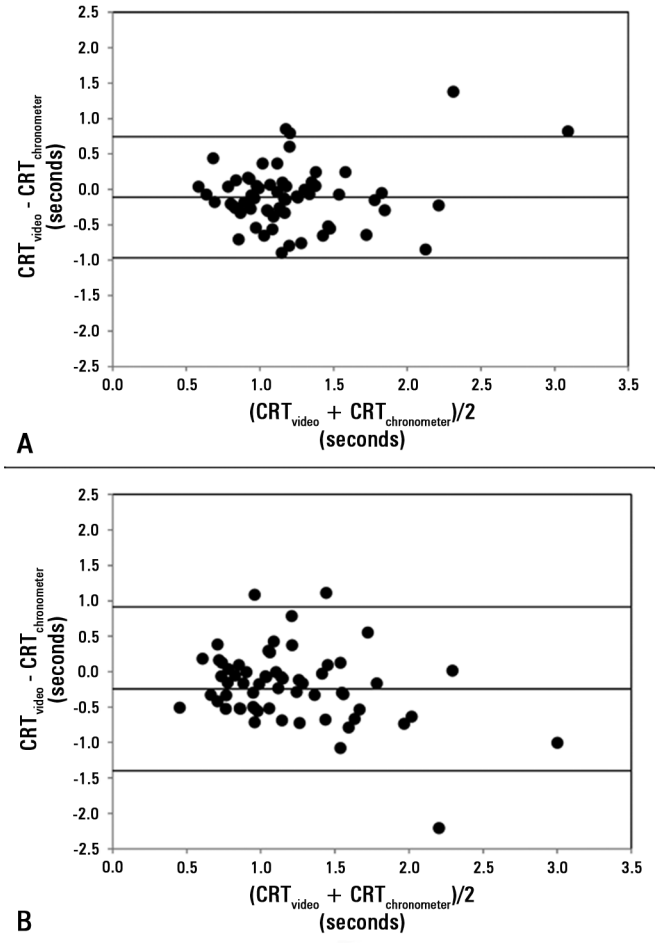

Figure 2 - Bland and Altman analysis for the agreement between measurements of capillary refill time performed by a chronometer during the direct visualization and by video analysis ($CRT_{chronometer}$ and CRT_{video}, respectively). Panel A shows the data from observer 1 and panel B from observer 2. Horizontal lines represent bias and 95% limits of agreement. CRT - capillary refill time.

using an arbitrary definition of 2 seconds as the upper limit of normality.[12] This cutoff point was confirmed by observational studies,[13] but there were concerns about its sensitivity and specificity.[14,15] CRT was thus eliminated from trauma assessment.[16] In an attempt to increase specificity, another guideline defined prolonged CRT as 3 seconds,[17] while studies in critically ill patients used even longer time frames.[2,18] Our results agree with the studies identifying the superior limit of CRT as approximately 2 seconds. Regardless of the observer and technique used for measurement, the superior limit of normality calculated from our results stayed within a narrow range of 2.0-2.7 seconds. In contrast to previous reports,[12,19] we did not find differences related to gender or age. One explanation for this finding is that we studied a group of relatively young people, with all volunteers younger than 65 years of age.

The poor interobserver reproducibility in the measurement of CRT was previously reported in some groups of infants.[5-8] Likewise, in a study performed in 6 adults, nurses exhibited moderate agreement in the determination of CRT.[20] A study performed in 207 clinically stable adults showed a lack of agreement in paired measurements of CRT.[9] This last result, however, is difficult to generalize because CRT was assessed without a chronometer, so the methodology used could explain the variability in the measurements.

Our results, obtained with an improved methodology, also showed poor interobserver agreement. Although still wide, the interobserver 95% limits of agreement in $CRT_{chronometric}$ were lower than those previously described (1.9 versus 3.6 sec), which might be ascribed to our improved standardized technique. Another explanation is that we only included healthy volunteers, who had lower CRT values than patients admitted to the emergency department, with expected derangements in peripheral perfusion. Consequently, lower and narrower values could have resulted in better precision (SD of paired differences).

This is not only the first report of interobserver agreement for $CRT_{chronometric}$ in healthy adults but also for CRT_{video}. Unexpectedly, we also found similar interobserver variability in the analysis of the video, most likely related to the difficulties of the human eye in assessing color changes, even during frame-by-frame examination on a computer screen. These drawbacks might hopefully be overcome by automated methods.[21]

In line with interobserver variability, the agreement between $CRT_{chronometric}$ and CRT_{video} measurements performed by the same observer was also poor. Despite high variability in the determination of CRT by different observers or methods, there were significant but weak correlations with other markers of skin perfusion. These findings emphasize that CRT might be a suitable approach for the evaluation of tissue perfusion. Moreover, clinical studies have shown that CRT can be useful as a prognostic tool.[2,22]

The correlation among different variables of peripheral perfusion has been previously reported. In critically ill patients, abnormal peripheral perfusion (defined as a skin cool to the examiner's hands or a CRT>4.5 seconds) was associated with increased temperature gradients and decreased perfusion index.[2] In critically ill pediatric

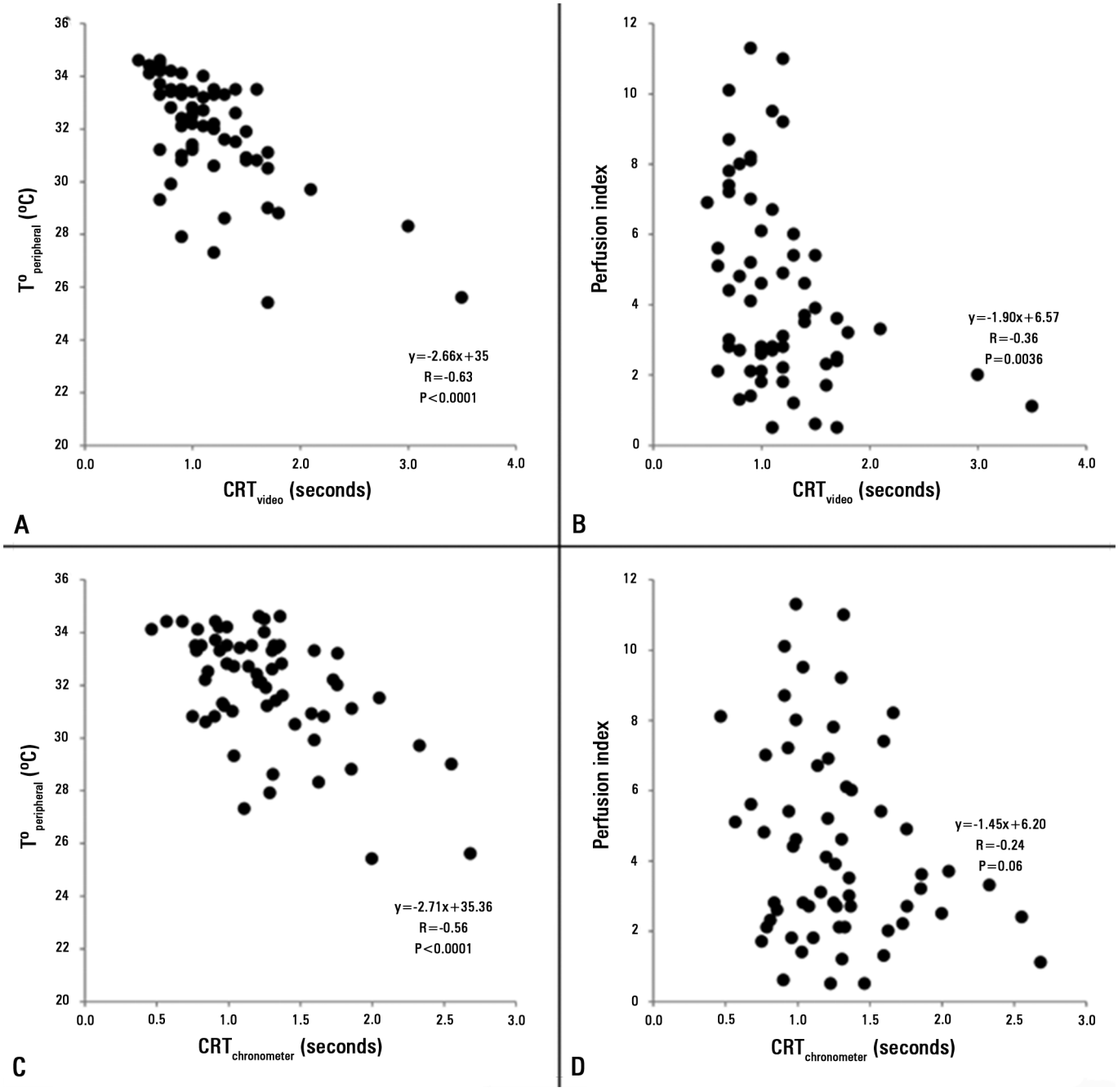

Figure 3 - Correlations among different variables of peripheral perfusion from data obtained from observer 1. Panel A: Correlation between capillary refill time performed by video analysis (CRT_{video}) and second finger pad temperature ($T°_{peripheral}$). Panel B: Correlation between CRT_{video} and perfusion index. Panel C: Correlation between capillary refill time measured by a chronometer during the direct visualization ($CRT_{chronometer}$) and $T°_{peripheral}$. Panel D: Correlation between $CRT_{chronometer}$ and perfusion index. CRT - capillary refill time.

patients, CRT was related to core-peripheral temperature gap,[23] also reported in cardiac surgery patients.[24] In healthy volunteers with normal peripheral perfusion, it might be more difficult to find correlations among perfusion markers because of the subtle changes that occur in the normal range. Nevertheless, we showed correlations of CRT with $T°_{peripheral}$ and perfusion index. The weakest correlations were observed with the perfusion index, possibly explained by the wide variation in its values. A large scattering of perfusion index in health volunteers was already reported,[25] although our results showed even higher mean values and dispersion

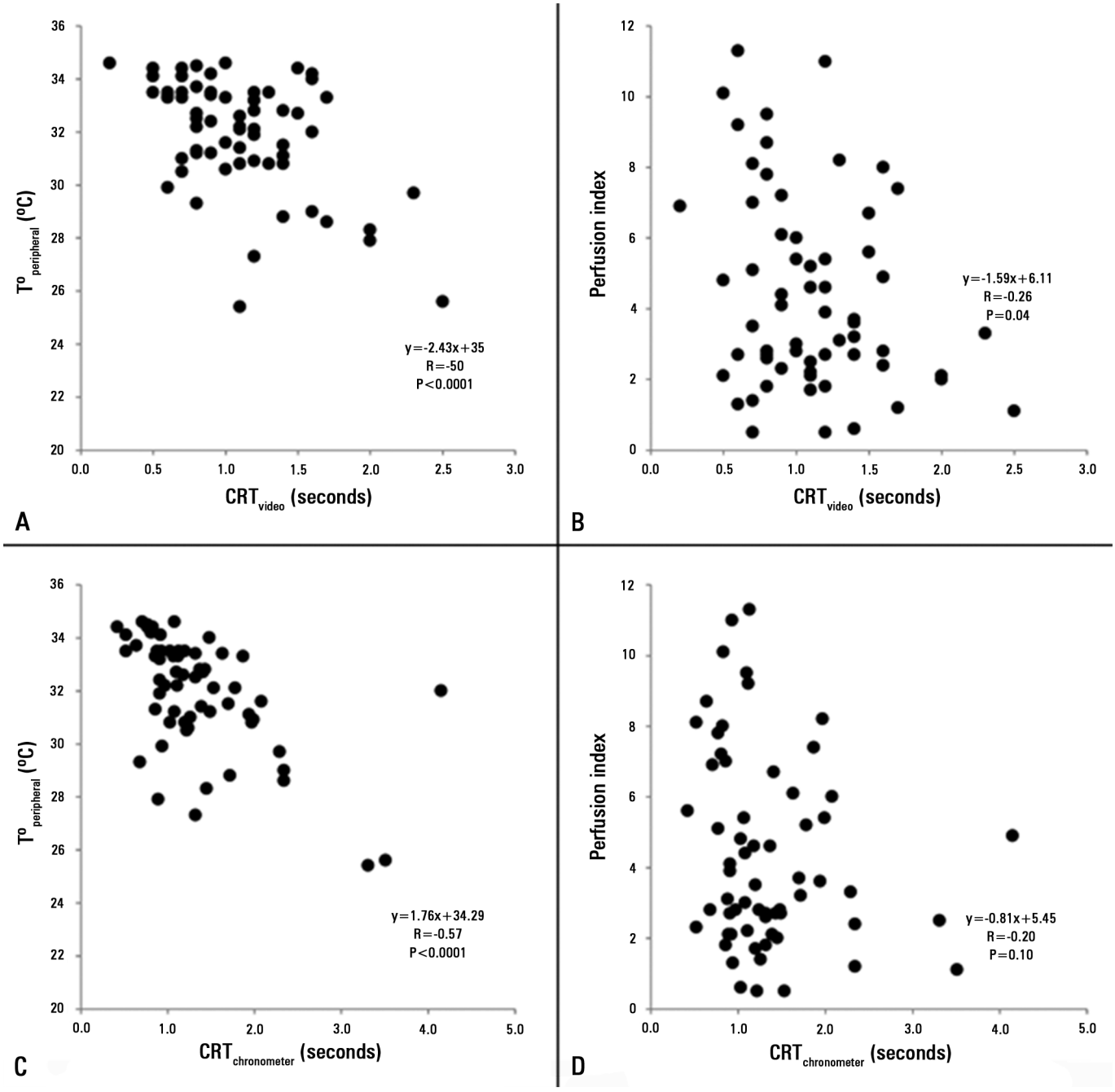

Figure 4 - Correlations among different variables of peripheral perfusion from data obtained from observer 2. Panel A: Correlation between capillary refill time performed by video analysis (CRT_{video}) and second finger pad temperature ($T^o_{peripheral}$). Panel B: Correlation between CRT_{video} and perfusion index. Panel C: Correlation between capillary refill time measured by a chronometer during the direct visualization ($CRT_{chronometer}$) and $T^o_{peripheral}$. Panel D: Correlation between $CRT_{chronometer}$ and perfusion index. CRT - capillary refill time.

(4.4±2.7 versus 2.2±2.0). The reason for this discrepancy is not evident but could be related to the susceptibility of the perfusion index measurement to movement artifacts.

There are controversial reports about the relationship of systemic hemodynamics to peripheral perfusion. In the first day after cardiac surgery and in cardiogenic shock, toe temperature and cardiac output were strongly correlated.[24,26] In septic shock, however, skin perfusion did not correlate with cardiac output,[25,26] most likely because the septic microcirculation could behave as

an independent compartment of the cardiovascular system.[27] In our healthy volunteers, $CRT_{chronometer}$ and CRT_{video} correlated with heart rate, but not with blood pressure. These results are expected because in normal subjects, cardiac output and tissue perfusion depend on heart rate and are independent of blood pressure.[28] In contrast to these findings in skin perfusion, one study showed that sublingual microvascular blood flow is affected by changes in blood pressure.[29]

Our study has limitations. First, we only studied a small sample of normal subjects without extreme values, which may be required for evaluation of the agreement between two methods. A larger sample size or the inclusion of critically ill patients could provide different results. Despite these limitations, the characterization of CRF variability in healthy volunteers is a required step in the development of knowledge about a physiologic variable used to monitor critically ill patients. Second, volunteers were only studied at rest. The evaluation of the dynamic response of CRT and of other indicators of peripheral perfusion to cardiovascular changes may be relevant. Third, intraobserver variability was not assessed.

CONCLUSION

In healthy volunteers, paired measurements of capillary refill time performed by different observers and methods showed wide 95% limits of agreement. The poor reproducibility should be considered not only in the evaluation of tissue perfusion in the individual patient but also in clinical studies. The weak correlation of the different measurements of capillary refill time with objective variables, however, suggests that capillary refill time is still a valid indicator of peripheral perfusion. Further studies are required to assess the reliability of capillary refill time measurements in critically ill patients.

RESUMO

Objetivo: As anomalias da perfusão periférica são manifestações importantes do choque, sendo o tempo de reenchimento capilar comumente utilizado em sua avaliação. Entretanto, a reprodutibilidade das mensurações do tempo de reenchimento capilar e sua correlação com outras variáveis da perfusão periférica não foram avaliadas de forma abrangente. Nosso objetivo foi determinar, em voluntários saudáveis, a concordância entre diferentes métodos e diferentes observadores na quantificação do tempo de reenchimento capilar, assim como sua correlação com outros marcadores da perfusão periférica.

Métodos: Estudamos 63 voluntários saudáveis. Dois observadores mediram o tempo de reenchimento capilar por meio de dois métodos distintos: visão direta ($TRC_{cronômetro}$) e vídeo-análise ($TRC_{vídeo}$). Medimos também o índice de perfusão derivado de pletismografia de pulso e a temperatura da polpa digital ($T^{o}_{periférica}$). A concordância entre os observadores e os métodos foi avaliada utilizando o método de Bland-Altman. As correlações foram calculadas utilizando a correlação de Pearson. Valor de $p<0,05$ foi considerado significante.

Resultados: Os limites de concordância de 95% entre ambos os observadores foram de 1,9 segundo para $TRC_{cronômetro}$ e 1,7 segundo para $TRC_{vídeo}$. Os limites de concordância de 95% entre $TRC_{cronômetro}$ e $TRC_{vídeo}$ foram de 1,7 segundo para o Observador 1 e 2,3 segundos para o Observador 2. As mensurações do $TRC_{cronômetro}$ realizadas pelos dois observadores se correlacionaram com a $T^{o}_{periférica}$. As mensurações do $TRC_{vídeo}$ realizadas pelos dois observadores se correlacionaram com a $T^{o}_{periférica}$ e o índice de perfusão.

Conclusão: As mensurações do tempo de reenchimento capilar realizadas por diferentes observadores ou diferentes métodos em voluntários saudáveis mostraram baixa concordância. Apesar disso, o tempo de reenchimento capilar ainda refletiu a perfusão periférica, conforme mostrado por sua correlação com variáveis objetivas da perfusão periférica.

Descritores: Choque/diagnóstico; Perfusão; Capilares/fisiologia

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