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The effect of pressure on capillary refill time

A clinical study on healthy volunteers

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Abstract

Introduction: Capillary refill time (CRT) has long been considered to be a measurement of cardiac output. Its role in modern medicine has been questioned and several factors have been proven to impact the length of CRT. Among these factors are: temperature, gender, age, pressure time and pressure site as well as the observers interpretation of CRT. In spite of this CRT is still used as a measurement of circulation.

Objective: To examine whether different pressures applied impacts the length of CRT or not.

Method: Two different pressures were tested on healthy adult volunteers. The two pressures were defined as just enough pressure to cause blanching of the tip of the observers thumb and one where the observer pressed as hard as possible without causing pain for the participant. Both pressures were performed in triplicates on the same person after which CRT was measured using a stopwatch.

Result: The mean difference between the two pressures was 0,4s (95% CI 0,29-0,50 $p < 0,0001$). Neither the CRT performed with light pressure nor the CRT performed with hard pressure showed an obvious symmetrical distribution.

Conclusion: A statistical significant difference between CRT as performed with the two different pressures was found. The difference in CRT between the two pressures found in this study was small and may not be clinical relevant, however the pressures used for CRT-measurements should be standardized, especially when conducting studies.

Abbreviations

CRT: Capillary refill time

CRT_L: Capillary refill time performed with light pressure

CRT_H: Capillary refill time performed with hard pressure

CV: Coefficient of variation.

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Introduction

Definition of Capillary refill time

Capillary refill time (CRT) has for a long time been considered to be a measurement of cardiac output. [1] The basic principle of CRT is that the practitioner presses, somewhere on the patient's body (preferably limbs, chest or head) enough to cause blanching of the skin and thereafter counts how many seconds it takes for the blanched area to regain its former color. [2-4] If CRT is delayed this could reflect a decreased cardiac output meanwhile a rapid CRT could be a characteristic of increased cardiac output. [1]

In 1947, Beecher et al described CRT as a response to blanching pressure. CRT was considered to be a part of recognizing shock and was defined as “normal”, “definite slowing”, or “very sluggish” which would correspond to “no”, “slight”, “moderate” or “severe” shock. No normal values were described and the evaluation of CRT was a subjective assessment by the clinician. [5]

Defining normal values

Champion et al defined immediate CRT as returning of color in less than 2s. This definition of normal CRT was not based on any experimental studies. [6,7] Discovery of normal upper values for men to be 2,0s, for women 2,9s and for the elderly population 4,5s respectively, made Schriger and Baraff propose a new cut off limit for normal CRT. The new normal values that were suggested were 2,0s for men, 3,0s for women and 4,0s for the elderly respectively. [8]

An Australian study from 2008 concluded that the cut of limit for healthy adults was 3,5s. The study did not account for the difference in CRT between men and women, yet it shows that an upper limit of 2s is inaccurate. [9] Regarding children, the upper limit of normal CRT has been shown to be 3s in neonates. [10,11]

CRT as a measurement of circulation

Altered tissue perfusion, which can be observed clinically, is an important manifestation of shock. Regarding the criteria for the clinical diagnosis septic shock, consensus was reached within pediatric emergency medicine in 2002. The criteria were hypothermia or hyperthermia together with clinical signs for decreased tissue perfusion such as altered mental status, CRT >2s, as in the case of cold chock, or shortened CRT, which would indicate warm chock, along

with other indicators for hypoperfusion. [12] Shock is a serious disorder which left untreated leads to death. The effect of shock is tachycardia, peripheral vasoconstriction and renal conservation of fluid. Among the circulatory changes is cutaneous vasoconstriction or vasodilation depending on the stage of shock the individual is in. [13]

Stroke volume index and lactate levels is other ways to measure perfusion. CRT has been shown to correlate with both stroke volume index and lactate levels. Lengthened CRT was linked to diminished stroke volume index and high lactate levels, which would reflect deficient perfusion. [14]

In addition to being a measurement of circulation, increasing CRT has been associated with increased mortality; however, other vital signs such as pulse, age and patient temperature correlates more closely with mortality. Nevertheless there are associations, although uncertain, between Schriger and Baraff's definition of CRT and mortality. CRT can be considered as a continuous method of measurement and such a point of view may be the most favorable. [15]

Another way to assess CRT is that a normal CRT may be a reassuring sign during ongoing treatment for septic shock. CRT has a role in predicting superior vena cava oxygen saturation above 70% in children, which is the targeted saturation according to guidelines, during septic shock resuscitation. [16]

Reproducibility of CRT

The reproducibility of CRT between different observers has been questioned [2] which a recent Argentinian study confirmed. However, an association between CRT and objective variables such as the peripheral temperature and perfusion index (estimated by pulse oximetry) was found, which indicates that CRT can be used as a measurement of peripheral perfusion. [3] In spite of the confirmed inter-observer variability, different observers tend to interpret normal and significantly increased CRT in the same manner. [4]

The study from 2014, performed by Ait-Oufella et al, attempted to standardize CRT measurements. This was achieved by instructing the physicians to apply enough pressure to cause blanching of his or her nail. This approach showed a good inter-observer reproducibility of CRT, especially when measured at the knee area. They conclude that CRT has a strong prognostic value in predicting 14-day mortality. [17]

Factors affecting CRT

CRT is affected by various factors: temperature, age and gender. Increasing temperature shortens CRT; with each 1°C increase, CRT decreases with 5%. CRT increases with age and men have a shorter CRT than women. No statistical significant correlation has been found between ethnicity, cardiac or antihypertensive medication and CRT. Gender, temperature and age account for an estimated 8% of the observed variability which indicates that there are additional factors affecting CRT. [9]

In addition to the variability in CRT with temperature, age and gender, the site for measuring influences the result. [18] Common practice is to blanch the nail bed of the patient's finger, [19] a site of measurement that has not been evaluated in studies. CRT as measured on the heel produces a higher value than measurements performed on the fingertip. [18] For practical reasons, in children, measurements at the midpoints of the forehead and sternum are preferred. These locations can be studied on children without patient cooperation being an issue. [11] Results obtained from the forehead and sternum showed low agreement. The CRT measured on the forehead was found to be shorter than the chest CRT values. This could be explained by differences in local skin blood flow. The measurements from hand and foot did not follow a Gaussian curve in contrast to CRT measured on chest and head. A possible explanation is difficulty in determining CRT as a result of poor patient cooperation. [10] When measured, CRT had a higher value at the dorsal surface of the foot than at the dorsal surface of the hand. [20] In addition to the varying results between measurement sites, CRT measured at the fingertip and at the chest is not comparable. [21]

The duration of pressure performed by the practitioner has been studied and it has been proven to impact CRT. However, when pressure applied lasts between 3 and 7s, the CRT is minimally affected. [11]

The diagnostic use of CRT has been debated [2] and its place in modern medicine, where more advanced and precise methods are available, has been questioned. [14] As mentioned above CRT has been shown to be affected by temperature, age, gender [9] and pressure time [11] as well as the subjectivity of the observer [3] and the site of measurement. [10] An area which have not been fully explored is if the amount of pressure exerted by the practitioner influences CRT. This is the focus of this study.

Aim

The objective of this study is to examine how different pressures exerted by the practitioner on the subject impacts CRT.

Hypothesis

There is a difference between CRT measured with light pressure (CRT_L) and CRT measured with hard pressure (CRT_H).

Null hypothesis

There is no significant difference between CRT_L and CRT_H.

Material and methods

The participants

This study was performed on healthy adult volunteers between the ages 18-65. The study was conducted between 20th November 2014 and 27th November 2014. During this period people were approached at the campus of the School of Medicine at Örebro University with a questionnaire. Additional subjects were recruited in the same manner from the staff at the Department of Pediatric Medicine at Örebro University hospital. If a person met the criteria for exclusion he or she was not enrolled. In total 55 persons was enrolled in the study. The exclusion criteria were: feeling sick at the day of measurements, known heart disease, hypertension or diabetes as well as taking any medication 6 hours before the study or being treated for any diseases at the time.

Ethical consideration

This was a non-invasive procedure that posed no threat to the participant's health or well-being; there was no obvious violation of the participant's personal integrity, which is why no application for ethical approval was submitted to the Regional Ethical Review Board. Every potential subject gave an oral consent after receiving information about the aim and method of the study. Every subject was informed that they could withdraw from the study at any point without stating their reason. The participants were presented with a questionnaire with questions regarding their health. Some questions could be inconvenient to answer (such as: are you being treated for any diseases?) and would exclude the subject from the study. Reading the questionnaire before agreeing to be part of the study gave the participants the

chance to withdraw without stating why or which question they answered in a way that excluded them.

The measurements

The measurements could not be performed in the same room every time, to account for the climate difference this could bring, the ambient temperature was measured two times for every subject, once before measuring CRT and once after. The rooms in which the measurements took place were well lit.

Before measuring CRT the temperature was measured with a commercially available thermometer. The subject put his or her hand on a table which put the hand in a position below heart level. CRT was measured on the dorsal side of the right hand with two different pressures, one where the practitioner pressed just enough to cause blanching of the tip of the thumb as Ait Oufella et al described in their study [17] (referred to in this paper as light pressure) and one where the practitioner pressed as hard as possible without causing pain for the subject (referred to in this paper as hard pressure). The pressures were measured alternatingly, starting with the light pressure. Both pressures were performed in triplicates and a mean value was calculated. The practitioner pressed for 5 s after which the time for the former color to return was measured with a commercially available stopwatch. There was a 30s waiting period between each measurement [10,11] to prevent warming of the skin. After performing the CRT measurements the temperature was measured again with the same thermometer.

Statistics

No other studies exploring the influence of the amount of pressure applied on CRT have been found which is why no power analysis was performed. T test was used on the difference between the CRT performed with light pressure and hard pressure. Coefficient of variation was calculated with the formula: $100 * (\text{Within subject SD})/\text{Mean}$. All calculations were performed in Microsoft excel as well as the creation of all figures and tables.

Results

The participants

The mean ambient temperature during measurements was 23,7°C (range 22,6-24,8°C). The age distribution was varied with the most subjects in the age 20-25, who represented 60% of the study population. The mean age was 24 with a range from 20 to 62 years old. . A total of 55 persons were included in the study, 32 (58%) women and 23 (42%) men, no one withdrew.

Capillary refill time

Neither the CRT_L nor the CRT_H showed an apparent symmetrical distribution as shown in figure 1.

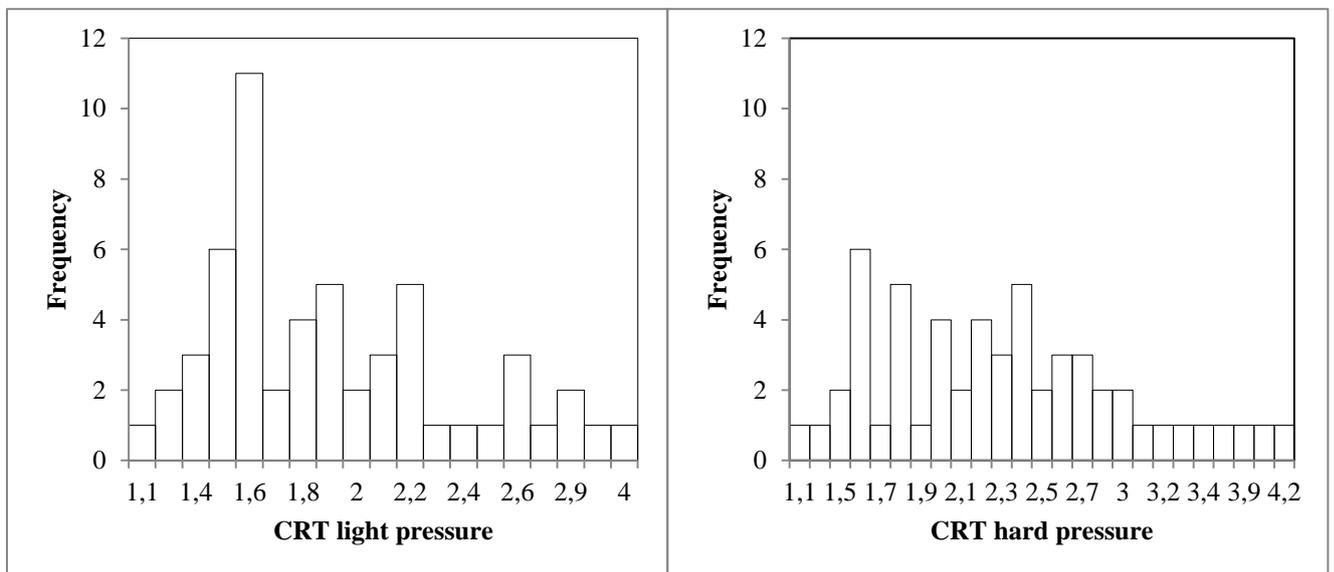


Figure 1: Histograms showing the distribution of CRT using light and hard pressure

The median for CRT_L was lower (1,80 s) than for CRT_H (2,28s). The box and whiskers plot in figure 2 shows the difference in results between the two measurement techniques. As a whole, the values for CRT_H were higher than CRT_L.

The mean difference between CRT_H and CRT_L was 0,40 s (95% CI 0,29-0,50, p<0,0001). The mean CRT_L was 1,95 ± 0,56(SD) (range 1,13 - 4,01). The mean CRT_H was 2,34 ± 0,69(SD) (range 1,13 – 4,23). The measurements, both using the light and the hard pressure showed a wide range and a scattered distribution.

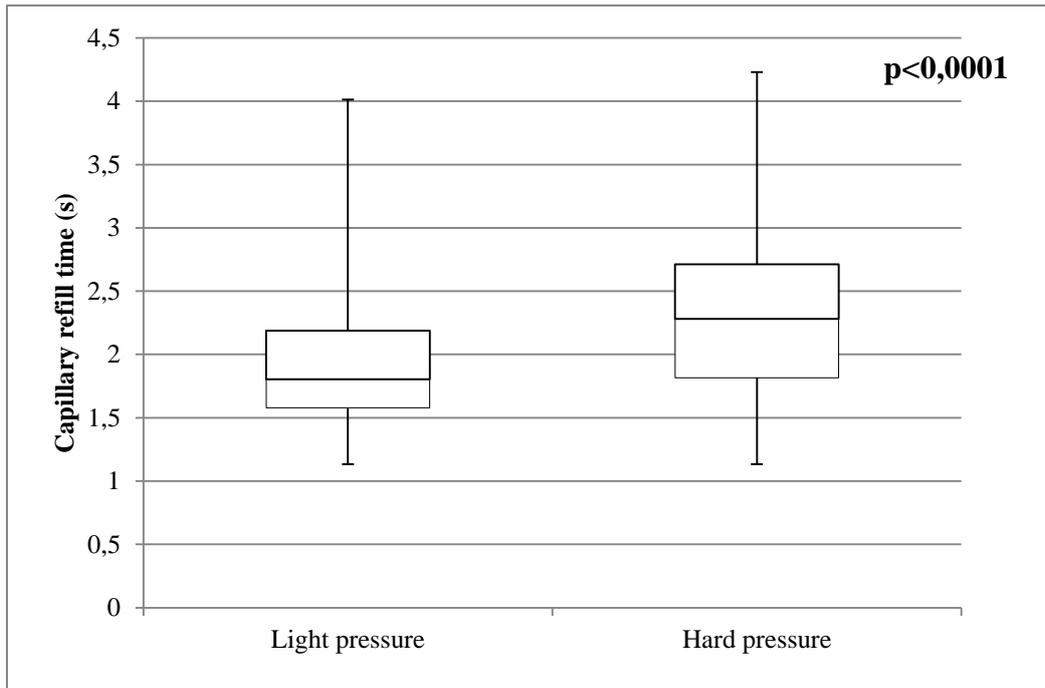


Figure 2: Box and whiskers plot (presenting the minimum value, 25th and 75th percentile, median and maximum value) overviewing CRT performed with the two pressures. The mean difference between the two pressures had a p value of <math>< 0,0001</math>.

No apparent association between age and CRT difference was seen as shown in figure 3, which is why no further statistical analysis was performed.

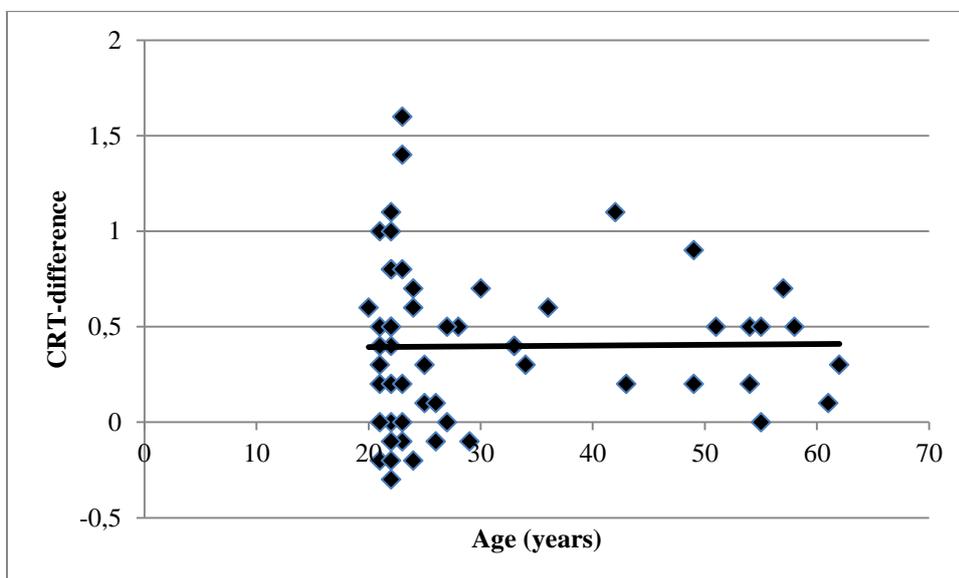


Figure 3: The CRT-differences correlation to age.

The mean for each of the six measurements tended to follow an order effect, with the highest being the first measurement, as presented in figure 4. The coefficient of variation (CV), a

measurement of the variation of all the values, for the light pressures was 16% and CV for the hard pressures was 15%.

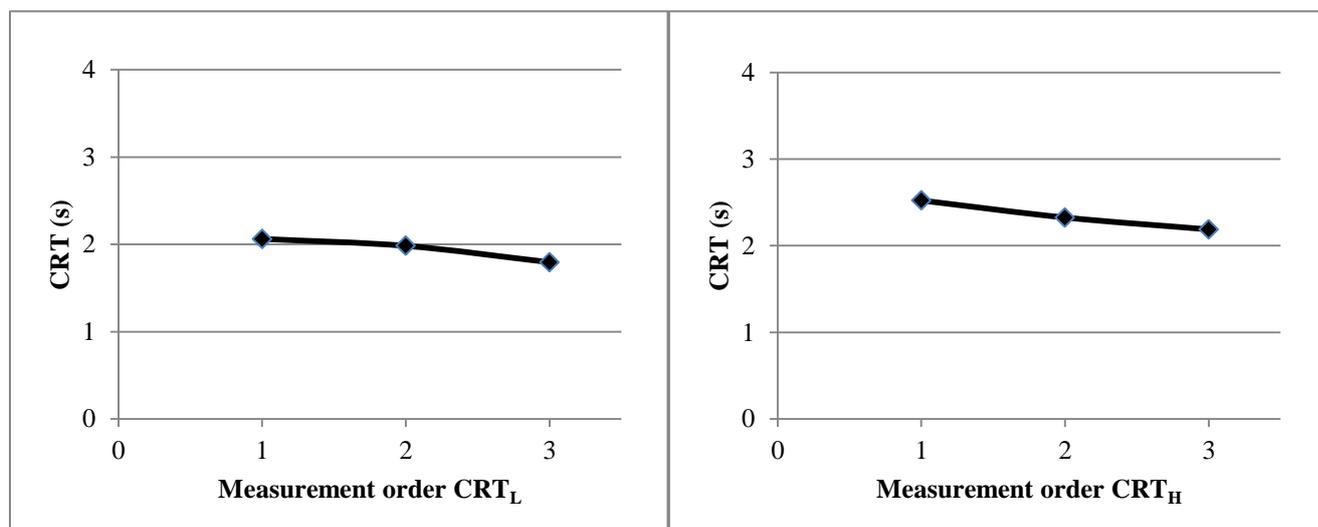


Figure 4: The impact of measurement order on CRT.

Classifying the participants

A classification of the participants using the different definitions is presented in table 1. Using the definition of normal proposed by Champion et al [6,7] (<2s) and the light pressure, 55% of the participants were misclassified and 64% using the same definition and the hard pressure. Schriger and Baraff's [8] definition (CRT \leq 2s for men, \leq 3s for women and \leq 4s for people over the age of 62) misclassified 15% of the participants (6% of the women and 26% of the men) using CRT_L and 38% (16% of the women and 70% of the men) using CRT_H.

Table 1: The percentage of participants classified as normal using the different definitions of normal.

Definition	Percentage classified as normal using CRT _L	Percentage classified as normal using CRT _H
Champion et al.	65%	36%
Shriger and Baraff (total)	85%	62%
Shriger and Baraff (Women)	94%	84%
Shriger and Baraff (Men)	74%	30%

Discussion

The present study aimed to examine whether the pressure applied impacts CRT or not. A statistical significant difference between the two pressures tested was found, hence the null-hypothesis can be falsified. Other studies to compare the difference with were not found. The

mean difference was 0,4s and although it is statistical significant it is not clearly clinically relevant. It is unlikely that a practitioner, not using a stopwatch, would perceive such a short difference. A perceivable difference would likely be a difference of at least 1 second. [10] Furthermore, in a clinical setting, the variance in pressure applied, might not be as big as in this study as a clinician generally does not apply as much pressure as he or she can. However, taken together with other factors that influence CRT such as temperature [9], pressure time [11] and site of measurements [10], the amount of pressure applied could produce a clinically relevant CRT-difference. Although questionably relevant in a clinical setting, how much pressure applied should be taken into account, when performing studies, as it impacts the CRT-results.

In this study 35% of the participants were considered abnormal using CRT_L and the 2s cut off. Using the hard pressure 65% were classified as abnormal. Set in comparison to 45% misclassified participants as seen in the study by Andersson et al. The rate of misclassification decreased to 19% [9] when using the Schriger and Baraff's [8] definition. When comparing this study's results of 15% (CRT_L) and 38% (CRT_H) to 19%, these numbers seem to correspond (disregarding the high misclassification when using hard pressure which is unlikely to be the standard pressure to apply in the study compared with). Such a high misclassification-rate indicates that these cut off limits does not represent a range where 95% of the population is included. A majority of the misclassified were male which suggest that a 2s cut off limit is unsuitable. The light pressure had a lower rate of misclassification whereby this method appears to be more suitable when measuring CRT. The definition of blanching of the observers thumb can be used to standardize the pressure when measuring CRT, when performing a study or in a clinical setting.

Neither the CRT_L nor CRT_H had a symmetrical distribution, a finding which shows consistency with others results [10]. The site of measurement has been explored in children, not as substantially in adults, which makes it difficult to compare this study's results with others. Nevertheless in children CRT in the hands in particular has shown a scattered distribution, which indicates that it may not be the preferable site to measure CRT at. In children the scattered results has been linked to a lack of cooperation. [10] A lack of cooperation by the participants cannot explain this study's result.

The tendency of an order effect seen in this study can be accounted to a warming effect of the skin which shortens CRT. [20] A 30s waiting period was applied before each test in an

attempt to prevent any warming. A waiting period of 30s may not have been sufficient in preventing the influence of heat from the observers thumb on the participant's skin. Since every CRT-measurement period started with testing the light pressure, the warming effect could have impacted the CRT_H more than CRT_L . However, increasing temperature shortens CRT and since the second pressure (CRT_H) measured would be more impacted than the first (CRT_L), because of the repeated contact of the observer's thumb with the participant's skin, this would lead to shortening of CRT_H and a less effected value of CRT_L . The difference in CRT was calculated as $CRT_H - CRT_L$, a shortened CRT_H would therefore produce a smaller difference, thus, the difference that was found cannot be attributed to the warming effect of the skin. Still, it is a weakness in the study and in future studies a randomized design could be applied where CRT_L is measured first in one group and CRT_H is measured first in another.

The hydration status of the subjects was not taken into account in this study. This could have influenced the results but as this study's aim was not to determine normal values for CRT, a moderately dehydrated person would have impacted both the CRT_L and CRT_H and therefore the difference between the two would remain the same, in other words this did not represent a differential bias. Furthermore, an exclusion criteria was feeling unwell at the time of measurements, this would eliminate individuals who were severely dehydrated.

The distribution of age amongst the participants could have impacted the results. Age impacts CRT in a way that CRT increases with increasing age. [9] However, this would likely impact both CRT_L and CRT_H which as in the case of hydration-status would not be a differential bias and it would not affect the difference between the two pressures. Nevertheless, the difference between CRT_L and CRT_H in different age-groups is not a well explored subject and therefore this factor cannot be disregarded.

To account for the effect temperature has on CRT, the temperature was measured at each measurement-time and it did not vary substantially. It would have been favorably to measure patient temperature, perhaps with a skin-thermometer. As shown previously, ambient temperature impacts CRT by an increase of 1,2% per degree Celsius. A bigger increase by 5% for every degree Celsius in patient temperature has been seen. [9] Patient temperature poses a greater problem, a clinician can, to some degree, control the environment for the physical exam but he or she cannot control patient temperature, although, it is questionable that the slight difference in patient temperature creates a real difficulty in a clinical setting. [9] The

ambient temperatures biggest range in this study of 2,2 °C (maximum-minimum) would only have had a small impact on CRT.

The inter-observer reproducibility of CRT has been explored, most studies have found a substantial difference between different observers. [2,3] In this study the same observer performed every test which eliminated the inter-observer variability, although, it may have introduced other biases as the observer was not blinded for the previous results when performing further measurements. Moreover, having only one observer put more reliability on the observer's ability to apply the same amount of pressure on all participants and to determine the endpoint of CRT. In future studies it may be suitable for the observer to be a senior practitioner with greater experience in performing CRT.

A variance in results of CRT of 16% (CRT_L) and 15% (CRT_H) was found which is well above the CV of 5% [22] that is commonly viewed as acceptable. The fact that it is difficult to reproduce CRT on the same individual might not be relevant in a clinical setting were CRT is usually only performed once. Still, it raises the question as to how suitable CRT is as a diagnostic tool, if the same observer cannot produce two similar values on a patient how can two measurements of CRT be compared?

A possible explanation for the high variance of CRT in this study is that it is difficult to determine the end point for the measurements. Another factor that should be taken into account is the pressure applied. The definition of the pressures as “blanching of the tip of the thumb” and “as hard as the observer can press” could have varied between the measurements. The definition “blanching of the tip of the thumb” is an interpretation, which is made by the observer and it is doubtful that the observer made the exact same interpretation every time. The definition “as hard as the observer can press” could vary between measurements as the observer might have tired after many measurements. Yet, regardless of how the pressures varied between measurements, there was a distinct difference between the two pressures which showed a difference in CRT. In a clinical setting the definition of pressure applied as “blanching of the tip of the observers thumb” could favorably be used as an attempt to standardize CRT measurements as seen before. [17]

Conclusion

In conclusion there are many factors that impact CRT, among them pressure, these factors as a whole poses a threat to the accuracy of CRT as a clinical finding. Therefore the results of

capillary refill should be interpreted with caution. In the authors opinion CRT should not be used as a separate diagnostic variable, but rather a finding that amongst others can be interpreted and used as basis for diagnosis and treatment.

The pressure applied should be defined as it affects CRT, as proven by this study. The lighter pressure is more suitable to use, in a clinical setting and in studies. Blanching of the tip of the thumb can be used as an indicator to prevent inter-observer and intra-observer variability. Standardizing the pressure used when measuring capillary refill time would improve the accuracy of this diagnostic tool.

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