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Long-Term Course of Haemoglobin and Ferritin Values in High-Frequency Donors of Whole Blood and Double Erythrocyte Apheresis

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High-frequency donors · Interdonation interval · Ferritin · Haemoglobin

Abstract
Background: High-intensity donation is a risk factor for iron deficiency in blood donors. Interdonation intervals for whole blood (WB) donation and double unit red blood cell apheresis (2RBC) vary among countries. We retrospectively evaluated the course of haemoglobin (Hb) and ferritin values in men regularly donating WB 4 times a year or 2RBC twice a year (i.e., maximal frequency) over a period of 48 months. ***Methods:*** Data of male donors with 16 WB or 8 2RBC consecutive donations were analysed. The minimum Hb levels for WB donation and 2RBC apheresis (collection of 360 mL RBC) were 135 and 140 g/L, respectively. There was no lower limit set for ferritin, and no iron was substituted. ***Results:*** We identified 294 WB (mean age 53 years, SD 11) and 151 2RBC donors (mean age 48 years, SD 9) who donated at a mean interval of 97 (SD 18) and 201 days (SD 32), respectively, between January 1, 2008, and December 31, 2013. At baseline, Hb and ferritin values were lower in WB donors compared to 2RBC donors, with a mean Hb of 153 g/L (SD 13) versus 159 g/L (SD 8) and a mean ferritin of 44 µg/L (SD 52) versus 73 µg/L (SD 56; $p < 0.001$ for both parameters), respectively. Ferritin was below 15 µg/L in 40 WB (14%) and in 4 (3%) 2RBC donors. In WB donors, the mean Hb levels at baseline versus last donation showed no significant difference (153 vs. 152 g/L, $p = 0.068$), whereas the mean ferritin levels decreased significantly (44 vs. 35 µg/L, $p < 0.001$). The 2RBC donor group displayed a statistically different decrease in both the mean Hb levels (158 vs. 157 g/L; $p < 0.05$) and the mean ferritin levels (73 vs. 66 µg/L; $p = 0.052$). The lowest Hb was measured at the 11th WB donation (152 g/L; $p < 0.05$) and at the 4th 2RBC apheresis (157 g/L; $p < 0.05$). There was no deferral due to low Hb at any time. The lowest ferritin was shown at the 4th WB (37 µg/L) and at the 3rd 2RBC donation (60 µg/L), respectively. At the last visit, ferritin was below 15 µg/L in 23 WB donors (8%) and in 2 2RBC donors (1%). ***Conclusions:*** High-intensity male donors with an interdonation interval of 12 weeks for WB donation and 24 weeks for 2RBC apheresis maintain acceptable Hb levels and, after an initial decline, stable ferritin levels despite ongoing blood donation.

Introduction

Due to the decreasing pool of active blood donors and the overall aging of the general population, one major challenge for blood banks will be to ensure a sufficient blood supply to patients [1]. To tackle this task, one strategy is increasing the frequency of blood donations by shortening the interdonation interval and thus collecting a greater number of blood units per donor. However,

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shorter intervals may expose blood donors to a higher risk of iron deficiency and deferral due to low haemoglobin (Hb) [2–4].

Iron deficiency is a major challenge for maintaining an active blood donor pool [5–7]. In the INTERVAL trial, the only randomised study conducted on the interdonation interval in whole blood (WB) donors, a blood donation frequency higher than the standard in the UK (12 weeks for men, 16 weeks for women) increased the number of blood products but also resulted in more frequent donation-related symptoms, deferrals due to low Hb and iron deficiency [5]. Strategies to prevent low Hb and iron deficiency anaemia, including a reduction of donation frequency, were implemented in many single institutions [8, 9] and are currently discussed at a regulatory level [10].

On the other hand, the introduction of longer interdonation intervals can have a negative impact on blood procurement [11], depending on the extent of the interval prolongation. Although the interval between donations is one of the strongest predictors of iron deficiency [12], current practices vary among national blood services as well as single blood collection facilities [13]. In the United States, both males and females are allowed to donate WB every 8 weeks and double red blood cells (2RBC) by apheresis every 16 weeks [14]. The European Directives require the same minimal interdonation interval (8 weeks) for WB donors and set a total limit of 6 and 4 donations yearly for males and females, respectively. At the same time, the Directives recommend 4 and 3 donations yearly for males and females, respectively, not to be exceeded. The minimum interval for 2RBC collection is 4 and 6 months for men and women, respectively [15].

Women of childbearing age, young persons aged 16–18 years, and high-frequency donors are at the greatest risk of iron deficiency. These donors are more often deferred due to low Hb and are more likely to cease donating blood permanently [7, 16]. However, there appears to be a small, not well defined subgroup of frequent donors who are able to maintain normal Hb levels despite low iron stores and repeated donations at the shortest interval possible [17].

In Switzerland, the minimum interval for WB donations is 10 weeks for both men and women, but following the European recommendations, the practice is to allow a maximum of 4 and 3 donations yearly, respectively. The interdonation interval for 2RBC apheresis is set at a "protective" frequency of 24 weeks for both sexes.

At our centre, the routine measurement of ferritin was implemented along with the introduction of 2RBC apheresis in January 2004. We performed a retrospective analysis of Hb and ferritin measurements in male blood donors who donated WB or 2RBC by apheresis at the maximum donation frequency of 4 and 2 times yearly, respectively, over a period of 48 months. The aim of the study was to describe the course of Hb and ferritin and the occurrence of deferrals due to low Hb in these high-intensity blood donors.

Materials and Methods

Subjects and Eligibility Criteria

In this study, regular male WB donors aged 18–75 years and 2RBC donors aged 18–65 years were included. Donor selection criteria in accordance with the Swiss regulations and the European Directives had to be fulfilled. Regarding the donors' age limits in Switzerland, eligibility of WB donors older than 65 years is subject to approval by a blood donation physician and may be extended up to the age of 75. These donors are required to undergo regular medical evaluations every 2 years assessing their individual risk profile. The upper age limit for donations by apheresis is 65 years.

All subjects in the 2RBC group must have at least 1 WB donation prior to their first 2RBC apheresis, and many of them were regular WB donors previously. Conversely, only a few WB donors had donated 2RBC by apheresis prior to the inclusion in the study. Complete data on the donation history was not available for every donor.

We searched our files for blood donors who donated at the shortest interval (12 weeks for WB and 24 weeks for 2RBC) and found that the highest donation frequency was maintained for a period of 48 months by the majority of these subjects, and therefore focused our analysis on this period. Thus, we identified 445 donors (3.8% of all male donors) who underwent 16 consecutive WB donations and 8 consecutive 2RBC apheresis over 48 months.

Platelet apheresis donors, those with hereditary haemochromatosis or any *HFE* gene mutation, if known, were excluded from the analysis. Also excluded were procedures that were not completed for any reason (i.e., because of local haematoma or technical issues).

The eligibility criteria for WB donors included a minimum Hb level of 135 g/L and a minimum body weight of 50 kg, while the 2RBC apheresis donors were required to have a Hb of at least 140 g/L and a body weight of at least 70 kg, approximately correlating with a total blood volume of 5 L or more.

Ferritin levels were not included in the eligibility criteria nor were they used for the selection of 2RBC donors. Thus, volunteers were accepted for WB or 2RBC donation independently of their iron stores. No iron supplementation was provided to donors at any time, but donors were not systematically asked whether they had any symptoms of iron deficiency or were taking iron supplements.

Laboratory Testing

At each visit, a complete blood count was performed from a pre-donation finger prick sample on a haematology analyser (Sysmex K-4500, Sysmex Digitana AG, Horgen, Switzerland). Ferritin was also measured at each visit from a venous blood sample collected at the beginning of each procedure with a chemiluminescence assay (Architect ci8200, Abbott Diagnostics, Abbott Park, IL, USA). Results were available the following day. Our ferritin reference ranges for men were 30–300 μg/L.

Donation Procedures, RBC, and Iron Loss

For conventional WB donation, a volume of approximately 450 mL blood was collected with an additional 30 mL blood (approximately 14 mL RBC) for routine testing. The corresponding total iron loss was about 240–260 mg, considering a loss of about 1 mg per 1 mL RBC [18]. The minimum interdonation interval was 12 weeks.

Table 1. Characteristics of the study population, number of donations and haemoglobin and ferritin values at the first and last donation of the observation period

	WB donors	2RBC donors	*p* value
Donors, *n*	21,700	495	
Male donors, *n* (%)	11,772 (54)[a]	495 (100)[b]	
Included in the study, *n* (%)	294 (1.3)[a]	151 (31)[b]	
Donations, *n*	82,324	2,394	
From male donors, *n* (%)	52,721 (64)	2,394 (100)	
From donors included in study, *n* (%)	4,704 (9)	1,208 (50)	
Donations prior to study, mean (SD), *n*	68 (40)[c]	40 (30)[d]	<0.001[f]
Mean interval (SD), days	97.4 (17.8)	201.0 (32.2)	<0.001[f]
Age, median (range), years			
At 1st visit	56 (20–70)	48 (23–63)	<0.001[g]
At last visit	60 (24–74)	52 (27–67)	
Hb			
At 1st visit, mean (SD), g/L	153 (13)	159 (8)	<0.001[f]
At last visit, mean (SD), g/L	152 (8)	157 (9)	<0.001[f]
Subjects with low Hbe, *n*	0	0	
Ferritin, mean (SD), µg/L			
At 1st visit	44 (52)	73 (56)	<0.001[f]
At last visit	35 (25)	66 (55)	<0.001[f]
Ferritin at 1st visit, *n* (%)			<0.001[h]
≥100 µg/L	18 (6)	38 (25)	
51–99 µg/L	48 (16)	49 (32)	
31–50 µg/L	85 (29)	44 (29)	
16–30 µg/L	103 (35)	16 (11)	
≤15 µg/L	40 (14)	4 (3)	
Ferritin at last visit, *n* (%)			<0.001[h]
≥100 µg/L	5 (2)	32 (21)	
51–99 µg/L	80 (27)	74 (49)	
31–50 µg/L	87 (30)	27 (18)	
16–30 µg/L	99 (33)	16 (11)	
≤15 µg/L	23 (8)	2 (1)	

[a] Of the whole WB donors population. [b] Of the whole 2RBC donors population. [c] Out of these, 5 donations were 2RBC apheresis. [d] Out of these, 43 donations were 2RBC apheresis. [e] Lower than 135 g/L for WB donors and lower than 140 g/L for 2RBC donors. [f] Independent sample *t* test. [g] Wilcoxon rank-sum test. [h] Fisher's exact test.

2RBC apheresis was performed with an ALYX device (Fenwal-Baxter, Zürich, Switzerland) programmed for the collection of 360 mL RBC, corresponding to approximately the RBC volume of two WB donations minus 40 mL. Taking into account additional RBC losses due to sampling for routine tests (about 30 mL WB, 14 mL RBC) as well as residual cells in the collection set (a median of 26 mL WB, about 11 mL RBC) [19], we calculated that the amount of iron lost at each completed 2RBC collection was approximately 385 mg. Thus, the amount of iron removed during each 2RBC apheresis (360 mL) was about 148% of that removed with each WB donation. The interval between two 2RBC aphereses was 24 weeks. No plasma or platelets were concomitantly collected.

Statistical Analysis

We used generalised estimating equation models of the Gaussian family with robust SEs in order to assess the temporal trajectories of WB and 2RBC donors' Hb and ferritin over 16 and 8 donations, respectively. Baseline Hb and ferritin at first donation were compared to subsequent measurements. Temporal changes in outcomes unadjusted and adjusted for age were reported both in the whole study cohort and in quartile groups defined by different Hb and ferritin values. Statistical significance was established at $p < 0.05$. A Stata version 15.1 (StataCorp, College Station, TX, USA) was used for all statistical analyses.

Results

Between January 1, 2008, and December 31, 2013, the overall number of WB collections at our centre was 82,324 from 21,700 donors. Of these, 11,772 were males (54% of all WB blood donors), who provided 52,721 WB donations (64% of all WB donations). The 2RBC donor pool comprised 495 male subjects and no females. The overall

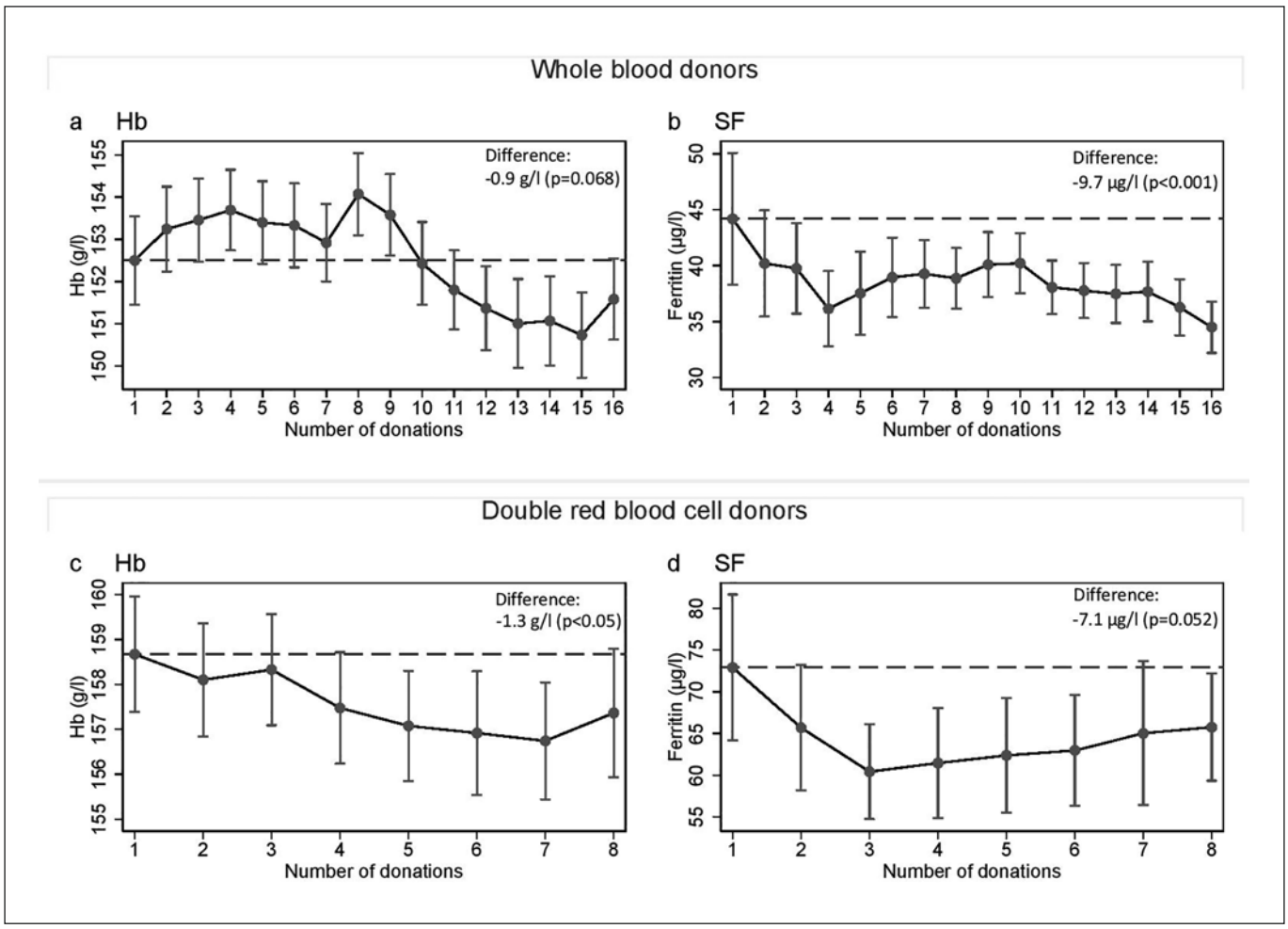

Fig. 1. Course of haemoglobin and ferritin in whole blood (**a–b**) and double red blood cell donors (**c–d**). Values are adjusted for age.

number of 2RBC aphereses performed within the study period was 2,394 (Table 1).

Characteristics of the Study Cohort and Values at the First and at the Last Donation (Table 1)

In the study cohort, there were 294 WB donors (1.3% of all male WB donors, 66% of the study population) and 151 2RBC donors (31% of all 2RBC donors, 34% of the study population). The cohort donors provided a total of 4,704 WB donations at a mean interval of 97.4 days (SD 17.8) and 1,208 2RBC aphereses at a mean interval of 201 days (SD 32.2).

At baseline, the 2 groups were different with respect to median age (WB donors: 56 years, range 20–70 years; 2RBC donors: 48 years, range 23–63 years; $p < 0.001$) and to the mean number of donations performed prior to the first procedure in the study (68 in WB donors and 40 in 2RBC donors; $p < 0.001$). In addition, both Hb (mean 153 g/L, SD 13 vs.159 g/L, SD 8) and ferritin (mean 44 µg/L, SD 52 vs. 73 µg/L, SD 56) were significantly lower in WB donors ($p < 0.001$ for both parameters).

While all donors fulfilled the Hb requirements, a broad range of ferritin values was observed in both groups. Ferritin was above 100 µg/L in 25% of 2RBC donors, but in only 6% of WB donors. The majority of WB donors (35%) had ferritin levels between 16 and 30 µg/L, while most 2RBC donors (32%) had values between 51 and 99 µg/L. Forty WB donors (14%) but only 4 2RBC donors (3%) had ferritin values below 15 µg/L indicating profound iron deficiency. Of the donors with very low ferritin values, those donating WB had a mean of WB donations prior to the study slightly lower than the overall mean of the WB group, while the 4 2RBC donors had a mean of previous WB donations that was higher than that of the whole 2RBC group (data not shown). Neither group had donated 2RBC by apheresis before the inclusion to the study.

At the last visit, the proportion of subjects with ferritin values between 16 and 30 µg/L slightly decreased (to 33%) in the WB group and remained unchanged in the 2RBC group. The percentage of donors with values below 15 µg/L dropped in both WB (8%) and 2RBC donors (1%).

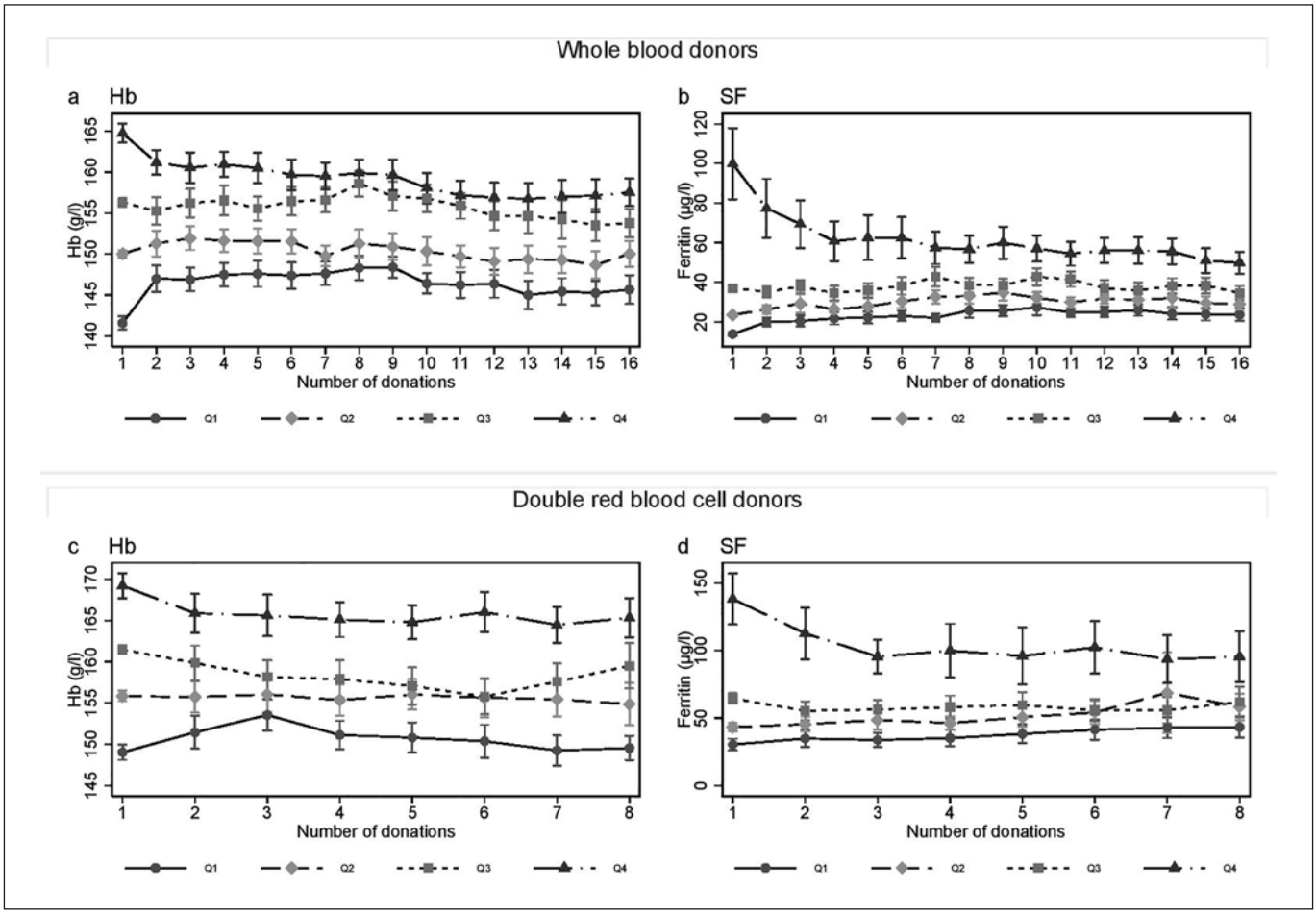

Fig. 2. Trajectories of haemoglobin and ferritin in whole blood (**a–b**) and double red blood cell donors (**c–d**) by quartile groups.

Course of Hb and Ferritin

Figure 1a–d shows the values of Hb and ferritin over a period of 48 months adjusted for age. In WB donors, Hb declined from 153 to 152 g/L ($p = 0.068$) and ferritin from 44 to 35 µg/L ($p < 0.001$), while in 2RBC donors Hb and ferritin decreased from 158 to 157 g/L ($p < 0.05$) and from 73 to 66 µg/L ($p = 0.052$), respectively. Hb and ferritin differences between donation groups remained stable, with substantially higher levels of both Hb (mean 5 g/L) and ferritin (mean 26 µg/L) in 2RBC donors. Compared to Hb at baseline, in WB donors a statistically significant Hb drop was observed from the 11th visit on (152 g/L, $p < 0.05$), that is, approximately after 33 months. Correspondingly, the lowest Hb values in 2RBC donors were observed from the 4th donation on (157 g/L, $p < 0.05$), that is, approximately after 24 months. Hb declined further in both groups until the 15th (minimal value: 151 g/L) and 7th donation (minimal value: close to 157 g/L), respectively, with an increasing trend afterwards. However, the Hb levels have never reached their baseline levels in either group within the 48 months. On average, Hb levels remained 5 g/L (95% CI 3.7–6.4, $p < 0.001$) higher in 2RBC donors compared to WB donors over the entire study period.

Ferritin levels in WB donors decreased from 44 µg/L at the first visit to 35 µg/L ($p < 0.001$) at the last donation, and in 2RBC donors from 73 to 66 µg/L ($p = 0.052$). Relative to baseline, a first significant ferritin drop in WB donors was observed already at the 2nd donation (41 µg/L), after approximately 3 months, followed by a second decline at the 4th visit, approximately 12 months later (37 µg/L, $p < 0.001$). From there on, a parabolic trend was observed, with a peak at the 10th donation and a consecutive drop (Fig. 1b). Similarly, ferritin significantly decreased in 2RBC donors at the 2nd donation (66 µg/L), after approximately 12 months, reaching the lowest level at the 3rd donation (60 µg/L) after 18 months. From that point, ferritin values increased and reached 66 µg/L ($p = 0.052$) at the end of the study period. Ferritin levels were also lower at the last visit compared to those at baseline in both groups, and were on average higher in 2RBC donors (mean 26 µg/L; 95% CI 19.3–32.7 µg/L; $p < 0.001$) over the entire observation period (Fig. 2b, d).

We further assessed the trajectories of Hb and ferritin in quartile groups (Fig. 2a–d). For WB and 2RBC donors alike, we consistently found that Hb and ferritin declined most steeply in subjects with the highest baseline values (Q4). In WB donors of Q4, Hb declined in the range of 3.5–8.0 g/L, while in 2RBC donors, the decrease was 3.3–4.7 g/L. The corresponding ferritin drop was in the range of 22.5–50.1 μg/L in WB donors and 25.5–44.6 μg/L in 2RBC donors.

Conversely, in donors with the lowest levels at first donation (Q1) values tended to improve with time. More specifically, Hb in Q1 significantly increased in the range of 3.7–6.0 g/L in the WB group and of 0.2–4.5 g/L in the 2RBC group, while the ferritin increase was in the range of 6.1–13.5 and 3.4–13.0 μg/L, respectively. As compared to Q1 and Q4, the 2 intermediate quartile groups (Q2 and Q3) displayed a more stable trajectory of both Hb and ferritin, and values showed smaller differences from those at baseline.

Discussion

This study describes the course of Hb and iron stores in a selected population of high-intensity male blood donors undergoing regular WB or 2RBC donations at the shortest interdonation interval recommended in Switzerland. Most interestingly, these subjects did not show a drop in Hb below the acceptance limit over the 4 years' period of donating on a regular basis regardless of their iron stores including profound iron deficiency (ferritin below 15 μg/L).

Previous large studies reported ferritin values lower than 10–12 μg/L in a substantial proportion of regular blood donors, ranging from 15% in the RISE study [20] to over 26% at our centre [9]. In the vast majority of WB donors, a minimum interval of 8 weeks, as currently adopted in the United States, is not sufficient for restoring Hb and iron stores, and is often associated with deferrals due to low Hb unless iron supplementation is given [12]. However, reducing the maximum donation frequency may not be alone sufficient to prevent relevant iron deficiency in blood donors. As shown by our data, despite a lower donation frequency in Switzerland compared to that of many other countries, ferritin values below 30 μg/L were found in over one-third (35%) of male donors and about 10% had values below 15 μg/L.

On the other hand, Mast et al. [17] described a self-selected population of 138 high-intensity male and female blood donors who did not develop anaemia despite very low ferritin levels. The mechanism of "resistance" to iron deficiency anaemia observed in these "superdonors" was not completely elucidated through extensive evaluation, including hepcidin measurement and testing for *HFE* mutations [17]. It is possible that a significant proportion of the donors selected for our study may share some characteristics of the above-mentioned superdonors. Considering that in the study by Mast et al. [17] the interdonation interval was 8 weeks, most subjects in our cohort may possibly tolerate even more frequent blood donation schedules than currently recommended in Switzerland (4 WB donations yearly). Similar postulations may apply to the interval between two 2RBC aphereses. Our procedure for 2RBC apheresis (collection volume of 360 mL and interval of 24 weeks) appears to be particularly protective regarding iron loss. Although previous studies showed an insufficient recovery of iron stores with intervals of 16 weeks in the absence of iron supplementation [21, 22], it is possible that many of the 2RBC donors in our cohort may tolerate aphereses at a 16-weeks' frequency without developing low Hb. With this respect, it is important to consider the differences in baseline characteristics of WB and 2RBC donors and also in the types of donation described in our study. 2RBC donors were younger, had higher Hb and ferritin levels at baseline, and had a lower number of previous blood donations (a mean of 40 vs. 68 in WB donors). These differences may be explained by the more recent recruitment of 2RBC donors following the introduction of 2RBC apheresis at our centre in 2004 as well as by different Hb cut-offs required for the 2 types of collections (140 g/L for 2RBC apheresis vs. 135 g/L for WB donation). Hb and ferritin levels in 2RBC donors remained higher throughout the observation period, which is most probably explained by the fact that the RBC volume and iron amount lost with 2RBC apheresis are less than that of two WB donations. Another interesting finding is that 2RBC donors were much more likely to donate at the maximum frequency compared to WB donors (31 vs. 1.3%). This data does not support the concern that a longer interdonation interval may induce a loss of motivation and a lower donor return [23].

The overall changes of Hb and ferritin observed within our study were similar in both types of blood donations. An initial drop in the values was followed by an upward trend later, even though the baseline levels of neither parameter were regained in neither group by the end of the study. Gonzàlez et al. [24] described a very similar course of ferritin in 2RBC donors over regular apheresis at an interval of 24 weeks. Also in that study, ferritin levels recovered after an initial significant decline, and so the authors concluded that ferritin is possibly not the most important parameter for 2RBC donor selection.

Since we included only experienced blood donors in the study, the number of previous donations had an impact on Hb and ferritin values at the baseline visit, but complete data on the donation history could not be retrieved for each donor. Therefore, we chose to analyse results separately in groups defined not by the number of previous donations but by baseline Hb and ferritin levels (quartiles). Particularly interesting is the favourable

course of Hb and ferritin in subjects starting with the lowest values (Q1) in both donation groups. One could hypothesise that this subgroup in particular shares some metabolic characteristics of the "superdonors." Identifying these subjects prospectively in a given donor pool is probably not possible. Indeed, in our study these subjects represented only a very small fraction of the WB and 2RBC donors (1.3 and 2.5%, respectively). However, we believe that these numbers underestimate the actual proportion of potential high-frequency donors who may provide a highest yield of blood products in the long-term. This aspect has a particular relevance when considering the generally declining number of active blood donors and the overall observed low donation frequency. At our centre, active blood donors represent about 4.1% of all potentially eligible adults living in our region, and give on average 1.5 donations yearly, for a total of about 15,000 WB donations yearly. The number of 2RBC apheresis is steeply declining (over 300 per year in 2008–2013 and 108 in 2018). During the period of our analysis, from 2008 to 2013, there was approximately 1 WB donation and 0.8 2RBC donations per year for the total donor population. As also discussed by Di Angelantonio et al. [5], identifying donors who best tolerate more frequent donations would provide a valuable tool for enabling more flexible interdonation intervals. Since it is evident that no fixed interval can be applied to all donors alike, defining individualised donation frequencies may be the most appropriate approach for retaining and protecting donors. However, such a strategy requires a more precise characterisation of the actual risk for iron deficiency and low Hb in distinct blood donor groups, as we attempted in our analysis.

Based on our observations, Hb and ferritin values display different courses in distinct groups of regular blood donors, which may have potentially significant implications for donor care. First, it allows for a more correct interpretation of the initial variations of values (e.g., steeper drop of ferritin in subjects starting at higher levels, as shown by our data). Second, it demonstrates that low ferritin does not necessarily impact sustained blood donation and requires no intervention in subjects with sufficient Hb levels. With this respect, however, it would be important to evaluate specifically the presence of iron deficiency-related symptoms in donors with low ferritin levels. It is important to consider that prolonged iron deficiency even in the absence of symptoms and despite normal Hb levels may possibly negatively impair donors' health. Although the long-term effects of iron deficiency without anaemia are still unclear and are most probably influenced by individual differences, repetitive blood donation in iron-depleted subjects may represent a potential harm. In addition, recent data, although not conclusive, indicate that also the quality of RBC products can be altered by the donor's low iron stores. In the study by Kanias et al. [25], donation intensity and ferritin levels correlated negatively with the RBC susceptibility to oxidative haemolysis during storage, but haemolysis was also mitigated if the donor received iron substitution. Another study in animal models demonstrated that RBC collected from mice with iron deficiency had a significantly shorter survival during storage and after transfusion [26].

A routine ferritin measurement creates undoubtedly valuable data that may help optimise donation frequency in individual donors [6]. This approach however cannot be easily put into practice in all blood donation facilities as it has logistic and financial implications. Prediction models for assessing the likelihood of donors' deferral due to low Hb using previous Hb levels and disregarding ferritin have been proposed [2, 6]. These tools may prove helpful to identify potential high-frequency donors. In our opinion, further studies are needed to validate such models in large cohorts and in different donor groups.

Our study has the limitations of a retrospective analysis. In addition, the study population is small and has clear selection bias. All subjects of the cohort were males, the vast majority were middle-aged with very few young donors, and all were experienced donors with a variable number of previous donations. Thus, our results cannot be generalised to other blood donor groups, such as females and in particular pre-menopausal women and donors younger than 25 years. It is also not known with certainty whether some donors of our cohort took iron supplements without our knowledge, and information on symptoms of iron deficiency was not systematically collected. On the other hand, the homogeneous characteristics of the study cohort as well as the consistency of management of donors over time represent the strengths of our analysis.

In conclusion, Hb and ferritin values reflect characteristic patterns in high-frequency male WB or 2RBC donors over time and indicate the possibility of increasing donation frequency in a subgroup of subjects, with clear advantages on the procurement of blood products.

Statement of Ethics

The approval for this study was granted by the Ethikkomission Nordwest- und Zentralschweiz, Project ID 2019-01752.

Conflict of Interest Statement

The authors have no potential conflicts of interest to disclose.

Author Contributions

L.I. and V.P.: conception of the study and writing of the manuscript. V.P. and Z.J.: data collection. T.V.: statistics. All authors: manuscript revision and final approval.

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