Health-related quality of life in children with newly diagnosed immune thrombocytopenia

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ABSTRACT

Despite its generally transient and benign course, childhood immune thrombocytopenia has a large impact on health-related quality of life. Recently published guidelines state that quality of life should be taken into account while making decisions on management in childhood immune thrombocytopenia. We, therefore, assessed health-related quality of life in children with newly diagnosed immune thrombocytopenia in a prospective multicenter study. One hundred and seven children aged 6 months-16 years (mean age 5.57 years) were included. We used Pediatric Quality of Life Inventory™ and Kids' ITP Tools questionnaires at diagnosis and during standardized follow-up. Scores on the Pediatric Quality of Life Inventory™ Core Scales were compared with those of healthy children. Relationships between health-related quality of life scores and treatment modality, bleeding tendency and course of the disease were examined. Kids' ITP Tools proxy reports and parent self-reports showed significant higher health-related quality of life scores in children who recovered than in children with persistent immune thrombocytopenia (at 3 months: Kids' ITP Tools parent self-report score 80.85 for recovered patients (n=69) *versus* 58.98 for patients with persistent disease (n=21), $P<0.001$). No significant differences in health-related quality of life were found between children with mild or moderate bleeding or between children who received intravenous immunoglobulin or children who were carefully observed. In conclusion, health-related quality of life of children with newly diagnosed immune thrombocytopenia is not influenced by treatment modality or bleeding severity, but only by clinical course of the disease. (Dutch Trial Register identifier: NTR TC1563)

Introduction

Immune thrombocytopenia (ITP) is an autoimmune disorder characterized by isolated thrombocytopenia (peripheral blood platelet count <100x10^9/L) in the absence of other disorders associated with thrombocytopenia.[1] Only 20-25% of children with ITP will develop chronic disease, currently defined as thrombocytopenia <100x10^9/L lasting for more than 12 months.[1] In the case of no or mild bleeding the management consists of careful observation and restriction of activities that carry a risk of severe bleeding, regardless of platelet count.[2] Severe bleeding, occurring in only 3-6% of children,[3] requires treatment with corticosteroids, intravenous immunoglobulin or anti-D immunoglobulin, either alone or in combination.

Despite the transient and often benign course of the disease, many clinicians observe that ITP has a significant impact on health-related quality of life (HRQoL).[4] Recently published management guidelines state that HRQoL issues should be taken into account while making decisions on management in childhood ITP.[2,5] However, these statements are based on clinical experience rather than results of research since HRQoL studies in childhood ITP are scarce. Recently, several clinical studies addressing HRQoL in children with ITP have been performed,[6-11] but large prospective studies with longitudinal generic as well as disease-specific HRQoL measurements are lacking.

For this reason we decided to study HRQoL as part of a prospective study in children with newly diagnosed ITP: the TIKI study (Therapy with or without Intravenous Immunoglobulin for Kids with acute ITP), a multicenter randomized clinical trial to determine whether early administration of intravenous immunoglobulin can prevent a chronic course of the disease. In this study, children receive either a single dose of intravenous immunoglobulin or careful observation and treatment only in the case of severe bleeding. The final results of the primary outcome of this study are awaited and have not been published yet. The aim of the current HRQoL study was to relate generic as well as disease-specific HRQoL scores of children with newly diagnosed ITP to type of treatment, bleeding severity and clinical course of the disease, to analyze changes in HRQoL scores over time and to compare generic HRQoL scores of children with newly diagnosed ITP with already published data from a reference group of Dutch school children.[12]

Methods

Patients

Children aged 3 months to 16 years with newly diagnosed ITP, a platelet count below 20x10^9/L and with mild to moderate bleeding were eligible for inclusion in the TIKI study. Patients were excluded if

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they had severe bleeding, received immunomodulating drugs within 1 month before diagnosis, suffered from conditions with a contraindication to intravenous immunoglobulin treatment or if comprehension of the Dutch language was insufficient to fill out the questionnaires. Within 72 hours after diagnosis, patients were randomized to receive either a single infusion of intravenous immunoglobulin (0.8 g/kg) or careful observation and treatment to raise the platelet count only in the case of severe bleeding. At diagnosis, after 1 week, 1 month, 3 months, 6 months and 12 months HRQoL was measured, laboratory studies were performed and clinical data including bleeding severity were collected. Mild bleeding was defined as skin bleeding only (adapted Buchanan bleeding score[13,14] 0-2), whereas moderate bleeding was defined as mucosal bleeding as well (adapted Buchanan bleeding score 3). All patients and parents who returned HRQoL questionnaires at at least one time point were included in this HRQoL study. Although the TIKI study has not finished recruitment yet, based on pre-defined yearly interim analyses, the steering committee decided to report on HRQoL outcomes after enrollment of 100 evaluable patients.

The TIKI study was approved by the intitutional review board of the University Medical Center Utrecht. All parents and patients aged 12 years and older gave written informed consent before inclusion. The study was registered in the Dutch Trial register (NTR TC1563) and conducted in accordance with Good Clinical Practice guidelines.

Health-related quality of life questionnaires

In accordance with general recommendations we combined generic and disease-specific HRQoL questionnaires.[15,16] Parents of all enrolled patients aged 2 years and older as well as children aged 7 years and older completed the Pediatric Quality of Life Inventory™ (PedsQL™) generic core scale questionnaire,[17-22] (HRQoL of the child reported by proxy and by children themselves) as well as the disease-specific Kids' ITP Tools (KIT), developed by Barnard and further refined by Klaassen and Blanchette,[23-25] (HRQoL of children by proxy report and child self-report) at the abovementioned time points. In addition we used the parental burden questionnaire, a validated part of the KIT (parent self-report). Table 1 presents the different questionnaires used for each age group. We only included PedsQL™ questionnaires if more than 50% of all items had been answered, according to the manual of the PedsQL™. Additional information on HRQoL questionnaires is provided in the *Online Supplement*.

For HRQoL reference data on Dutch children, we used PedsQL™ data gathered in 496 Dutch children, aged 5-18 years, attending primary or secondary school. These data were published elsewhere and kindly provided by the authors.[12]

The age-specific questionnaires were handed in hard copy to parents and patients during their study visits and were filled out in the waiting room or at home. Local investigators sent completed questionnaires by mail to the coordinating investigator. Data were entered in an electronic database by researchers of the coordinating study center not aware of clinical data such as bleeding tendency, platelet count and treatment arm.

Statistical analysis

Since HRQoL scores were not normally distributed, Mann-Whitney tests were performed to analyze differences in HRQoL scores between two groups. For analysis of changes in HRQoL scores over time we used the repeated-measures ANOVA test, despite the non-normal distribution of data, as the repeated-measures ANOVA is fairly robust to deviations from normality. *P* values <0.05 were considered statistically significant. IBM SPSS version 20 was used for all analyses.

Results

Patients' characteristics

Enrollment started in May, 2009. Sixty hospitals opened the study at their institutions and 35 enrolled at least one patient. At the time of analysis, 125 patients were included in the TIKI study. HRQoL data were available for 107 patients, 53 boys and 54 girls with a mean age of 5.57 years (range, 6 months - 16 years). No patients were excluded because of insufficient comprehension of the Dutch language. Fifty-five patients received intravenous immunoglobulin, 52 were randomized to the observational arm. HRQoL scores at each timepoint including response rates are displayed in Table 2. No statistically significant differences were found between patients with or without available HRQoL data regarding gender, age, treatment arm, bleeding tendency and platelet count at diagnosis (*data not shown*).

PedsQL™ and KIT scores of children who received intravenous immunoglobulin and those randomized to the observational arm

The results of this comparison are shown in Table 3. At 1 week and 1 month, there were no significant differences in PedsQL™ total scores (proxy and child self-report) or KIT scores (parent self-report, child self-report and proxy report) of children who received intravenous immunoglobulin compared to scores of children randomized to the observational arm of the study. Likewise, PedsQL™ physical summary scores and psychosocial summary scores did not differ (*data not shown*).

PedsQL™ and KIT scores of children with mild versus moderate bleeding at diagnosis, 1 week and 1 month after diagnosis.

These results are shown in Table 4. There were no differences in PedsQL™ total scores (proxy and child self-report) or KIT scores (parent self-report, child self-report and proxy report) between patients with mild bleeding and patients with moderate bleeding at diagnosis and 1 week. Physical and psychosocial summary scores of the PedsQL™ did not differ either. At 1 month after diagnosis, the num-

Table 1. Questionnaires used in different age groups.

Age group	N.	PedsQL™ questionnaires	KIT questionnaires
0-1 year	18		parent self-report
2-4 years	49	proxy report 2-4 years	parent self-report proxy report
5-6 years	12	proxy report 5-7 years	parent self-report proxy report
7 years	3	proxy report 5-7 years child self-report 5-7 years	parent self-report proxy report child self-report
8-12 years	14	proxy report 8-12 years child self-report 8-12 years	parent self-report proxy report child self-report
13-16 years	11	proxy report 13-18 years child self-report 13-18 years	parent self-report proxy report child self-report

PedsQL™: Pediatric Quality of Life Inventory generic core scales; KIT: Kids'ITP Tools; N: number of participants. Age group 0-1 year denotes all children untill they reach the age of 2 years. This is applicable for all age groups.

ber of patients with moderate bleeding was too small (n<10) to perform reliable analyses.

PedsQL™ and KIT scores of children who recovered within 3 or 6 months and children with thrombocytopenia persisting beyond 3 or 6 months after diagnosis

The results regarding scores in patients who recovered and those who did not are shown in Table 5. PedsQL™ proxy total scores of children who recovered were significantly higher than those of children with persistent disease at 6 months but not at 3 months. Parent self-report and proxy report KIT scores of children who recovered within 3 or 6 months were significantly higher than those of children with persistent ITP beyond 3 or 6 months. There was no difference in KIT and PedsQL™ scores of children reported by themselves except for the KIT child self-report at 6 months, which showed a borderline significant difference between recovered patients and patients with persistent disease.

In the KIT parent self-report, questions with the largest difference in scores between persistent and recovered patients were questions regarding uncertainty of clinical course as well as questions regarding fear of bleeding and injuries. In the KIT proxy report the largest differences in scores were found for questions regarding uncertainty of clinical course, fatigue and not being able to participate in activities. In the KIT child self-report the largest differences in scores were found for questions regarding going to the hospital and having blood tests, as well as not being able to participate in activities.

Changes of PedsQL™ and KIT scores over time

HRQoL scores during follow-up are shown in Table 2. PedsQL™ and KIT scores analyzed by ANOVA tests improved significantly during follow-up (P<0.001). By performing subgroup analyses, we observed that HRQoL scores only improved in recovered patients, except for the KIT parent self-report scores that also improved in patients with persistent thrombocytopenia (Figure 1A-E).

PedsQL™ scores of children with immune thrombocytopenia versus those of the Dutch reference group

PedsQL™ scores of children with newly diagnosed ITP at diagnosis were comparable to PedsQL™ scores of the reference group of Dutch children reported by proxy [age 5-7 years, TIKI (n=11) median score 85.87 (range, 70.65-96.74) *versus* reference group (n=92) median score 85.87 (range, 59.78-98.91), P=0.81) as well as reported by children themselves (age 8-16 years, TIKI (n=19) median child self-report score 82.61 (range, 42.05-100.00) *versus* reference group (n=390) median score 82.61 (range, 56.52-100.00), P=0.60]. Since the impact of the disease might not have been completely realized at diagnosis, we also com-

Table 2. Overall HRQoL scores during follow-up.

	Diagnosis		1 week		1 month		3 months		6 months		Trend
	n. (%)	mean (SD)	n. (%)	mean (SD)	n. (%)	mean (SD)	n. (%)	mean (SD)	n. (%)	mean (SD)	ANOVA
PedsQL™ proxy report	70 (79)	84.74 (11.40)	70 (79)	83.56 (12.06)	72 (81)	87.88 (10.73)	75 (84)	90.52 (11.29)	70 (79)	91.90 (11.21)	P<0.001
PedsQL™ child self-report	23 (82)	82.46 (13.67)	17 (61)	81.34 (11.50)	22 (78)	86.05 (12.44)	18 (64)	90.67 (11.60)	22 (78)	91.04 (11.84)	P<0.001
KIT parent self-report	91 (85)	48.36 (17.01)	89 (83)	54.55 (16.83)	87 (81)	67.08 (18.76)	90 (84)	75.74 (19.05)	75 (70)	83.45 (15.61)	P<0.001
KIT proxy report	69 (82)	75.01 (14.18)	68 (76)	75.10 (13.96)	72 (81)	83.59 (12.66)	76 (85)	87.74 (11.07)	65 (73)	91.29 (9.29)	P<0.001
KIT child self-report	22 (78)	71.02 (14.35)	20 (71)	69.87 (15.70)	23 (82)	82.35 (12.10)	21 (75)	86.29 (11.17)	20 (71)	90.02 (11.32)	P<0.001

n.: number of completed questionnaires; %: percentage response; SD: standard deviation (in parentheses).

Table 3. HRQoL scores in the observation group *versus* those in the group treated with intravenous immunoglobin.

	1 week					1 month				
	Observation		IVIg			Observation		IVIg		
	n.	median (range)	n.	median (range)	P	n.	median (range)	n.	median (range)	P
PedsQL™ proxy report	31	80.56 (56.25-100.00)	39	85.87 (57.50-100.00)	0.10	35	89.13 (55.56-100.00)	37	90.91 (50.00-100.00)	0.18
PedsQL™ child self-report	10	88.04 (48.81-95.83)	7	80.43 (69.57-86.96)	0.31	13	95.65 (51.32-100.00)	9	83.70 (73.91-95.65)	0.16
KIT parent self-report	41	52.88 (27.88-90.38)	48	52.88 (12.50-89.42)	0.59	39	69.00 (20.19-100.00)	48	71.59 (21.15-95.19)	0.68
KIT proxy report	31	73.08 (45.00-99.04)	37	75.96 (51.92-100.00)	0.25	32	83.65 (47.12-97.12)	40	89.50 (48.96-100.00)	0.07
KIT child self-report	13	69.00 (53.85-100.00)	7	56.73 (42.31-94.23)	0.21	14	86.06 (61.54-100.00)	9	76.92 (61.54-96.15)	0.34

n.: number of completed questionnaires; IVIg: intravenous immunoglobulin.

pared the PedsQL™ scores of ITP patients 1 week after diagnosis with reference data. However, these comparisons showed the same picture (*data not shown*). Physical summary scores and psychosocial summary scores did not show any differences either (*data not shown*). Comparison of PedsQL™ scores of children with ITP persisting beyond 6 months with reference data was not possible because of the very small numbers of children aged 5-16 years with persistent disease (n=3 for children aged 5-7 years and n=4 for children aged 8 years and older).

Discussion

In this prospective multicenter study, we have shown that HRQoL in children with newly diagnosed ITP is not influenced by treatment modality or bleeding tendency, but only by the clinical course of the disease.

Many clinicians observe that newly diagnosed childhood ITP has a significant impact on patients and their families.[4] Children may feel restricted in their activities and parents may have fear of severe bleeding. Both children and parents may feel embarrassed by large skin bleeds. Recent management guidelines state that HRQoL issues should be taken into account while making decisions on management in childhood ITP.[2,5] However, these statements are based on clinical experience rather than results of research since HRQoL studies in childhood ITP are scarce.

Neunert *et al.* studied data from the KIT validation database with data from 90 children and related KIT scores to bleeding severity and platelet count.[6] They found no correlation between platelet count and HRQoL and only a weak, non-significant, correlation between bleeding severity and KIT scores. Klaassen *et al.* studied HRQoL using the KIT in 22 children with chronic ITP participating in a pilot study of romiplostin for children with chronic ITP.[7] Parents of children receiving romiplostin (n=17) showed significant improvement of KIT scores, whereas parents of children receiving placebo did not (n=5; *P*=0.008). Zilber *et al.* performed a retrospective cross-sectional study in 17 Israeli children with newly diagnosed and persistent ITP and 34 parents of children with ITP.[8] They found a significantly lower KIT score in parent self-reports than in child self-reports (*P*<0.001). Whether the disease was acute or chronic had no impact on the KIT score in either group. Grainger *et al.* performed a secondary analysis of the KIT validation database (n=217) to compare HRQoL between children managed with therapy to increase the platelet count and children monitored without therapy.[9] They found that HRQoL was not improved by treatment. However, since HRQoL was not measured before as well as after institution of treatment and treatment was not randomly assigned,

Table 4. HRQoL scores in patients with mild bleeding *versus* those with moderate bleeding.

	Diagnosis					1 week				
	Mild bleeding		Moderate bleeding			Mild bleeding		Moderate bleeding		
	n.	median (range)	n.	median (range)	*P*	n.	median (range)	n.	median (range)	*P*
PedsQL™ proxy report	41	87.50 (47.50-100.00)	27	85.53 (65.28-100.00)	0.75	56	84.78 (56.25-100.00)	14	81.25 (56.52-100.00)	0.16
PedsQL™ child self-report	15	82.61 (42.05-95.83)	7	86.96 (53.57-100.00)	0.89	14	84.78 (48.81-95.83)	3	83.79 (79.35-92.39)	0.86
KIT parent self-report	55	47.12 (16.35-91.35)	36	48.56 (16.35-84.78)	0.80	74	53.85 (12.50-90.38)	15	48.96 (27.88-86.00)	0.35
KIT proxy report	41	75.00 (33.00-100.00)	28	78.90 (51.92-93.00)	0.81	55	75.96 (51.92-100.00)	13	75.00 (45.00-95.19)	0.18
KIT child self-report	14	67.30 (44.23-91.35)	8	79.33 (52.88-96.15)	0.16	15	67.31 (42.31-100.00)	5	69.00 (55.77-94.23)	0.27

Mild bleeding: skin bleeding only, bleeding score 0-2. Moderate bleeding: mucosal bleeding as well, bleeding score 3; n.: number of completed questionnaires.

Table 5. HRQoL scores of recovered patients *versus* patients with persistent ITP.

	3 months					6 months				
	Recovered		Persistent ITP			Recovered		Persistent ITP		
	n.	median (range)	n.	median (range)	*P*	n.	median (range)	n.	median (range)	*P*
PedsQL™ proxy report	59	95.24 (57.61-100.00)	16	91.67 (51.19-100.00)	0.14	59	96.43 (57.95-100.00)	11	88.04 (52.50-100.00)	0.03
PedsQL™ child self-report	15	94.57 (79.35-100.00)	3	90.22 (48.75-96.59)	0.50	18	96.19 (68.75-100.00)	4	87.73 (54.55-95.65)	0.08
KIT parent self-report	69	83.65 (49.04-100.00)	21	60.58 (18.27-95.19)	<0.001	65	89.42 (40.38-100.00)	10	70.19 (38.46-86.54)	0.002
KIT proxy report	59	92.31 (54.81-100.00)	17	87.50 (51.92-100.00)	0.03	55	95.19 (77.88-100.00)	10	85.09 (47.12-100.00)	0.02
KIT child self-report	16	93.27 (68.27-100.00)	5	86.62 (60.58-93.27)	0.15	17	96.15 (77.88-100.00)	3	78.00 (52.88-91.35)	0.05

n.: number of completed questionnaires.

HRQoL could have been worse in treated children before the start of therapy and could even have influenced treatment decisions. Strullu *et al.* assessed PedsQL™ scores, but not KIT scores, in 73 French children with ITP at diagnosis, after 1 month, 3 months and 6 months.[10] They found that biological factors such as sex, age, platelet count, bleeding scores, bone marrow aspiration and persistence of ITP at 6 months were not significantly associated with PedsQL™ scores and concluded that disease-specific questionnaires, such as the KIT, should be used in future studies. Finally, Mokhtar *et al.* recently published a cross-sectional study in 80 Egyptian children with ITP using the KIT questionnaires.[11] They found that patients with newly diagnosed ITP had significantly lower mean scores than those with chronic ITP regarding parent self-report, child self-report and proxy report scores and that bleeding severity was inversely correlated with HRQoL scores.

In this study, we prospectively gathered HRQoL data using the generic PedsQL™ as well as the disease-specific KIT questionnaires at diagnosis and during standardized follow-up visits and related these scores to treatment arm, bleeding score and clinical course. Furthermore, we com-

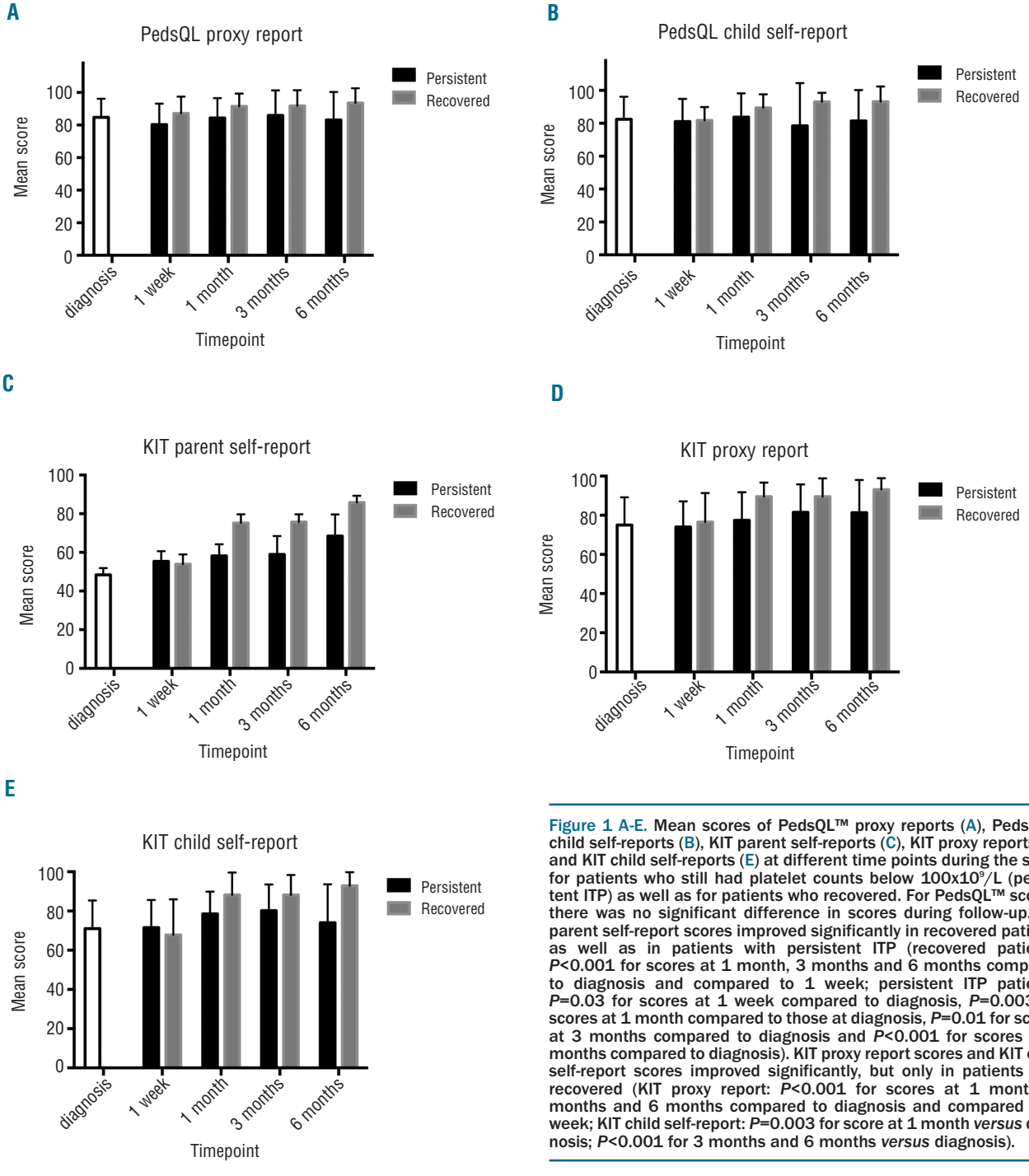

Figure 1 A-E. Mean scores of PedsQL™ proxy reports (A), PedsQL™ child self-reports (B), KIT parent self-reports (C), KIT proxy reports (D) and KIT child self-reports (E) at different time points during the study for patients who still had platelet counts below $100x10^9$/L (persistent ITP) as well as for patients who recovered. For PedsQL™ scores, there was no significant difference in scores during follow-up. KIT parent self-report scores improved significantly in recovered patients as well as in patients with persistent ITP (recovered patients: $P<0.001$ for scores at 1 month, 3 months and 6 months compared to diagnosis and compared to 1 week; persistent ITP patients: $P=0.03$ for scores at 1 week compared to diagnosis, $P=0.003$ for scores at 1 month compared to those at diagnosis, $P=0.01$ for scores at 3 months compared to diagnosis and $P<0.001$ for scores at 6 months compared to diagnosis). KIT proxy report scores and KIT child self-report scores improved significantly, but only in patients who recovered (KIT proxy report: $P<0.001$ for scores at 1 month, 3 months and 6 months compared to diagnosis and compared to 1 week; KIT child self-report: $P=0.003$ for score at 1 month *versus* diagnosis; $P<0.001$ for 3 months and 6 months *versus* diagnosis).

pared these scores with scores of a reference group of Dutch school children.

No differences were found in HRQoL scores between children with skin bleeding only and children with mucosal bleeding as well. These results are comparable to those of the study by Neunert *et al.*[6], but contrast with those of the study by Mokhtar *et al.*[11] The latter difference could be attributed to the different bleeding score used as well as to the different ethnic and cultural background of their study population.

At the start of our study, we hypothesized that treatment with intravenous immunoglobulin would improve HRQoL, because of the increased platelet count observed in the majority of patients treated this way and a concurrent lower risk of bleeding. However, we did not find any differences in HRQoL between patients in the intravenous immunoglobulin treatment arm and those in the observational arm of our study. This is concordant with the results of Grainger *et al.*[9] The impact of having an intravenous cannula and being hospitalized for several hours when treated with intravenous immunoglobulins may counterbalance a potentially positive effect of treatment on HRQoL scores in these children. Based on our study, improving HRQoL as a sole reason for intervention with intravenous immunoglobulins, instead of careful observation, in children with newly diagnosed ITP might be questionable. Since our study does not comprise treatment modalities other than intravenous immunoglobulin, we cannot provide any information on the effect of other treatment modalities on HRQoL.

We observed significantly higher KIT scores (parent and proxy) in children who did recover within 3 or 6 months compared to those in children who did not recover. This result seems to contrast with those of the study by Zilber *et al.*, who did not find any differences in scores between acute and chronic ITP patients[8] and the studies by Mokhtar *et al.*[11] and Klaassen *et al.*,[24,25] who found higher KIT scores in patients with chronic disease compared to those in patients with newly diagnosed ITP. However, the prospective design of our study seems to be better suited to answer this study question than the cross-sectional design of the studies by Zilber *et al.*, Mokhtar *et al.* and Klaassen *et al.* There are several potential explanations for the higher KIT parent self-report and proxy report scores we observed in children with ITP who recovered. People may have a better HRQoL when restrictions in activities are no longer necessary. Secondly, parents may feel relieved if their child has recovered from ITP and is considered to be healthy again. We did not find a significant difference in HRQoL reported by children themselves, but only five children aged 7 years or older developed persistent ITP, so very limited data were available to shed light on this issue. In patients with persistent disease, only KIT parent scores improved over time. Getting used to the disease and the limitations and fears associated with it as well as repeated and careful explanation of the disease, risk of bleeding and natural history of ITP may contribute to the improvement of HRQoL. However, clinicians should be aware of the impact of ITP on the HRQoL of both parents and patients and consider referring those with low scores for professional support. To investigate whether childhood ITP influences HRQoL in general, we compared PedsQL™ scores of newly diagnosed ITP patients with those of a reference group of healthy Dutch school children. PedsQL™ scores of newly diagnosed ITP patients and their parents did not differ significantly from those of this reference group. The reason for these findings could be that the PedsQL™ addresses only general HRQoL items, such as the ability to walk and visit school, which are not restricted in most patients. Relatively unaffected scores on generic HRQoL questionnaires are also seen in children with other hematologic conditions, such as hemophilia A.[26] ITP-specific HRQoL issues are only addressed in the KIT questionnaire, which was not administered to healthy children. Indeed, KIT scores at diagnosis and 1 week after diagnosis showed a relatively low HRQoL, especially in parents (Table 2).

Our study is not only the largest HRQoL study in children with ITP, it is also the first study reporting prospectively collected HRQoL data at several timepoints during the course of the disease using generic as well as disease-specific questionnaires. Finally, this is the only study comparing a randomly assigned intervention and careful observation as a management strategy in children with newly diagnosed ITP.

Of course, the study has some limitations. Because of the relatively young age of our study population, we were dependent on proxy reports regarding HRQoL of the children and could only gather HRQoL data of children themselves in the minority of patients. Treatment modalities other than observation and intravenous immunoglobulin were not studied, so this study could not provide any information on HRQoL in children treated with corticosteroids or anti-rhesus D immunoglobulin. Likewise, no information is available on HRQoL of patients with a bleeding score of 4 or 5, since such patients were not included in our study. Bleeding scores could not be related to HRQoL scores at time points later than 1 month, because the reported intervals differed too much. Finally, response rates were limited to 60-70% at certain time points, particularly for the child self-report questionnaires. Future research should take these limitations into account.

In conclusion, HRQoL in children with ITP is not influenced by bleeding severity or treatment modality, but only by the clinical course of the disease. Parental education and support along the course of the disease may contribute to an improvement of HRQoL.

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