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Insulin pump failures: has there been an improvement? Update of a prospective observational study

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Abstract

Background: Insulin pump failures had been assessed in our center by a prospective observational study from 2001 to 2007. The aim of this study was to update our data since 2008 and to determine if there exist specific risk factors for insulin pump failures.

Methods: All insulin pumps defects were prospectively collected between 2008 and 2013 in a monocentric cohort of 350 new pumps. Clinical consequences were recorded. Brand and model of pumps, type of defects and patients' characteristics (gender, age at diabetes diagnosis, age at first pump, pump treatment duration, number of previous pumps and number of previous pump failures) were tested for possible association with insulin pump failure.

Results: Malfunctions occurred in 239 (68%) pumps. The incidence rate was 33/100 pump-years. There were 28 (12%) complete failures, 17 (7%) alarms, 83 (35%) mechanical defects and 105 (44%) minor defects. Survival curves did not differ according to pump brand and model. Hyperglycaemia occurred in 2.9% of cases. In multivariate analysis, only patient age under 40 at the initiation of pump therapy was associated with higher risk of malfunction (HR 1.64; 95% CI 1.19-2.24; p=0.002).

Conclusions: Pump malfunctions remain common with modern pumps. We report less complete failures than in our previous study. This could be due to improvement in pumps or to our strategy of systematic screening and replacement in case of mechanical defects.

Abbreviations: CSII = Continuous subcutaneous insulin infusion; AIRB = Air de Bretagne

Background

Continuous subcutaneous insulin infusion (CSII) therapy has been used for nearly 40 years¹ and is an efficient and flexible treatment to improve both glycaemic control and quality of life²⁻⁴. However, insulin pump dysfunctions may have severe consequences^{5,6}. In spite of this, the clinical studies required by regulators prior to marketing new insulin pumps are limited and insufficient data is made publicly available on their long-term use in real-life setting⁷. We had determined the rate of insulin pump failure, excluding problems linked to infusion set defects, by a prospective observational study⁸. During this six-year study (2001-2007), 36% of our pumps broke down after a median time of 15 months. The current study was undertaken to update our data. The aim was to reassess the rate and the clinical consequences of pump defects and to establish whether some patients' characteristics are associated with an increased risk of malfunctions.

Methods

We prospectively studied the defects occurring between June 2008 and December 2013 on new insulin pumps used in ambulatory CSII. We included all pumps acquired between June 2008 and December 2011 by our partner, AIR de Bretagne (AIRB), a not-for-profit association in charge of the maintenance and supply of pumps.

Each CSII treatment had been initiated in an inpatient setting. Patients were given a choice between pumps manufactured by Medtronic (Paradigm® 512/712, Paradigm® 522/722, Paradigm® Veo™), Animas® (20/20) and Roche (Accucheck® Combo). They followed a specific education program including management of pump malfunctions. They were instructed to check glycemia in case of pump failure and ketones when glucose level was higher than 250mg/dl. The proper functioning of each component of the pump was systematically checked by healthcare professionals during at least four visits per year, and by patients themselves.

Pump users benefited from a 24/7 on-call medical service provided by diabetologists and a 24/7 technical hotline provided by AIRB.

The study focused on malfunctions directly related to the pump itself (and not infusion set problems), reported by the patient or identified during visits. According to the regulation on pump therapy in France, patients could not contact the manufacturer directly. Defects were always managed by AIRB and confirmed by the pharmacists in charge of surveillance devices. They were classified as: 1) complete failures that made pumps immediately unusable (blockage, continuous alarms, fixed screens and piston defects), 2) alarms that required pump replacement as recommended by the manufacturer, 3) mechanical defects (tank or battery-chamber crack, pad dysfunction), 4) minor defects (other pump cracks and display defects). Complete failures and alarms were considered as severe failures.

The occurrence of hyperglycaemia > 250mg/l, presence of ketones, severe hypoglycaemia} and need for hospitalization were prospectively recorded in case of severe failure.

We expressed quantitative variables as median and interquartile range. We compared continuous variables with the Student *t* test or Wilcoxon rank-sum test and discrete variables with the Khi-square test or Fisher's exact test, as appropriate. Pump survival was estimated with the Kaplan–Meier method and compared with a log-rank test. The parameters tested for possible association with pump failure were brands and pump models, types of failure and patients' characteristics (gender, age at diabetes diagnosis, age at first pump, CSII treatment duration, number of previous pumps and number of previous pump failures). A multivariate Cox proportional hazards analysis was performed to determine the independent predictors of pump failure. Values of $p < 0.05$ were considered significant. Analyses were performed using R statistical software, version 3.2.2.

Results

During the inclusion phase, 350 new pumps were acquired: 241 (69%) Medtronic pumps, 74 (21%) Animas and 35 (10%) Roche pumps. The pumps were used by 248 adult diabetic patients (162 women, 86 men; median age 47 years [36 - 60]; median age at diagnosis of diabetes 18 years [11 - 28]; median age at CSII initiation 33 years [25 - 47]). There were 213 (86%) type 1, 15 (6%) type 2 and 20 (8%) secondary or undetermined etiology diabetes.

Malfunctions occurred in 239 (68%) pumps. Median survival time was 26 [IQR: 16-39] months (Fig. 1a). The rate of malfunction was 33 per 100 pump-years. There were 45 (19%) severe pump failures (28 complete breakdown and 17 alarms set off); 83 (35%) mechanical malfunctions, 105 (44%) minor defects, cause was missing in six events (Table 1). Complete failures occurred earlier than other defects (13.5 [5-17.7] months versus 20 [11-27] months for alarms set off, 19 [13-26] months for mechanical defects and 24 [16-29.2] months for minor defects) ($p = 0.0056$) (Fig. 1b). All the damaged pumps were sent back to manufacturers who did not contest the defect.

There was no significant difference in survival curves according to pump brand and model (Fig. 1c). However, Medtronic pumps were more liable to mechanical defects ($p < 0.001$), Paradigm® 522/722 pumps to minor defects ($p < 0.001$) and Paradigm® Veo™ pumps to alarms ($p < 0.001$) (Table 1).

Throughout the study, 174 patients (70 %) experienced a pump defect, on one (71%), two (22%) or more (7%) occasions. Neither type and duration of diabetes, duration of CSII treatment, number of previous insulin pumps, nor number of previous pump failures were associated with higher risk of breakdown. Female patients (HR = 1.40, 95% CI 1.06-1.86; $p=0.017$) and those aged under 40 at the initiation of CSII (HR = 1.59, 95% CI 1.23-2.05; $p=0.0003$) (Fig. 1d) were more likely to experience pump failure. In multivariate analysis, only age under 40 at the initiation of CSII remained significant (HR 1.64; 95% CI 1.19-2.24; $p=0.002$) (Supplementary material table 2).

Mean HbA1C levels were similar in patients with or without pump defect ($7.9\% \pm 1.13$ versus $7.9\% \pm 1.37$; $p = 0.7$), and whatever the cause of malfunction ($7.7\% \pm 1.0$ for complete failure versus $7.9\% \pm 1.22$ in other defects; $p=0.53$).

Six episodes of hyperglycemia (13%) occurred following a severe pump failure ($n=45$), which represents 0.47 events per 100 patient-years. No case of ketosis, hypoglycaemia or hospitalization has been recorded in relation to severe pump failure.

Conclusions

Our prospective observational study on pumps used in ambulatory CSII treatment over 5 years has shown a defect rate of 33/100 pump-years. Malfunctions were severe in 19% of cases but have had clinical consequences in only 13% of cases.

To our knowledge, our previous study carried out between 2001 and 2007 and the current update are the only prospective studies of pump defects reported after systematic verification by healthcare professionals, which was not supported by the manufacturers. In most countries patients contact directly the manufacturers in case of malfunction. According to the FDA reports 1996-2005, Cope reported 1,594 events related to insulin pumps⁶. Other published data were obtained using phone interviews or questionnaires filled in by patients at the time of the incident⁹ or subsequently^{10,11}. Data were mostly collected over short periods. Defect rates reported were 27/405 patients/16 weeks⁹ 46%¹⁰ and 48% of patients¹¹.

Comparison with our first study suggests a lower proportion of severe (19% versus 72%). This may indicate an improvement of the pumps. However, we observed an increase of 32% in the pump replacement rate (33 versus 25/100 pump-years), mainly due to a mechanical and minor defects increase. Mechanical and minor defects in fact represented 35% and 44% respectively in this study, versus 18% and 9% in our previous study. We stress the considerable fragility of

the outer shell and the keyboard, being the cause of 35% of the defects observed, mainly cracks. As mentioned in instruction manuals, cracks in the reservoir or battery compartment may lead to short-circuits or leakage. Based on these results, we recommend assessing the functioning of these pump components at each visit and instructing patients to do this, particularly after a pump impact or in case of water contact.

Interestingly, major breakdowns appeared earlier than less serious defects. This result agrees with the findings of Pickup¹¹ who attributed it to the inexperience of novice patients. Another hypothesis could be a manufacturing defect leading to breakdown during the first year of use. Among our patients, in multivariate analysis, the only predictive factor of pump malfunction was age under 40 at the initiation of CSII. In order to explain this result, it could be important to collect data on other characteristics such as environmental factors, or psychosocial issues differing between generations. These factors (compliance, education, sports-related activities...) have already been suspected of contributing to adverse events in adolescent diabetic patients^{6,9}. This needs to be confirmed in adults before personalization of education programs according to the patient's age.

Complications related to severe failures, were less frequent than in 2007 and seem to be less serious than those appearing in other studies^{6,9,12}, probably because problems linked to the infusion set have not been included. In contrast with our results, Scaramuzza reported higher levels of HbA1c in breakdown cases¹⁰. As suggested by the authors, a potential loss of confidence in the technology may happen in breakdown cases and might have an impact on glycaemic control⁹.

The present study has intrinsic limitations. This "real-life" study does not allow a randomization by pump brand with an imbalance distribution in each brand. The statistical power was reduced by the late inclusion of some pumps resulting in a shorter duration of follow-up. A multicenter evaluation covering a larger population of pumps and patients would be useful.

In conclusion, defects in insulin pumps remain a common issue in clinical practice. These findings suggest the importance of systematic screening in order to promote the prevention of serious breakdowns and their clinical repercussions. The reliability of pumps is even more crucial as they are to be used as part of an artificial pancreas.

Legends:

Table 1: Number of pump defects (n) and time before defect (t) according to pump model and type of defect. P-values were calculated for each type of defect comparing pump models.

Figure 1: Pumps survival curves. 1a-Overall survival time, with a median of 26 months. 1b- Survival according to failure type, n = 239, log-rank p-value = 0.0056. 1c- Survival according to pump models, n = 350, log-rank p-value = 0.058. 1d - Survival according to age at pump initiation, n = 350, log-rank p-value < 0.0001. All survival analyses were censored at the time of the pump defect or day of the last observation on December 31, 2013.

Author disclosure statement: the authors declare that there is no conflict of interest associated with this manuscript.

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Fig. 1a - Overall survival time, with a median of 26 months

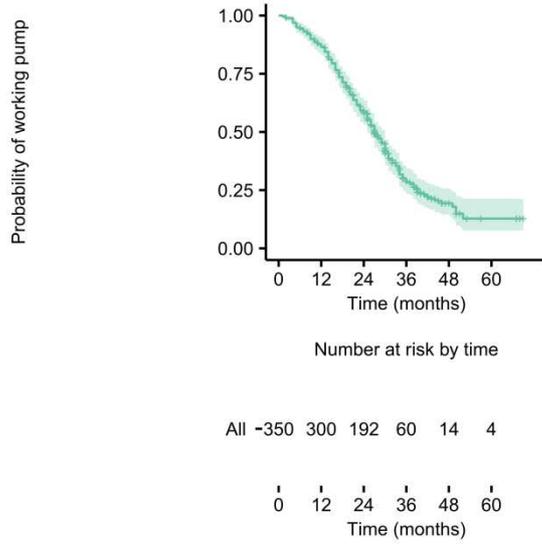


Fig. 1c - Survival according to pump models

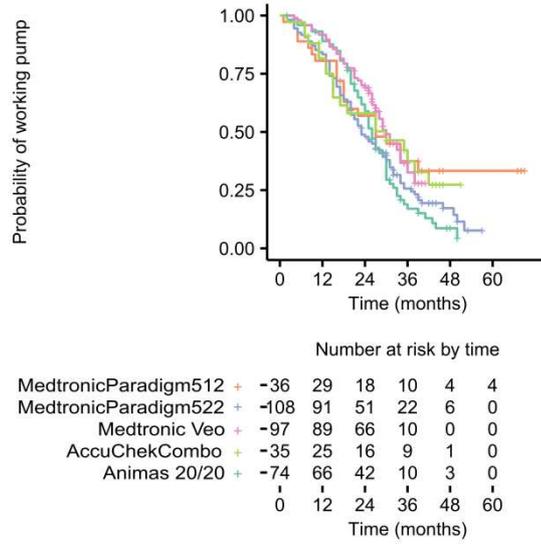


Fig. 1b - Survival according to failure type

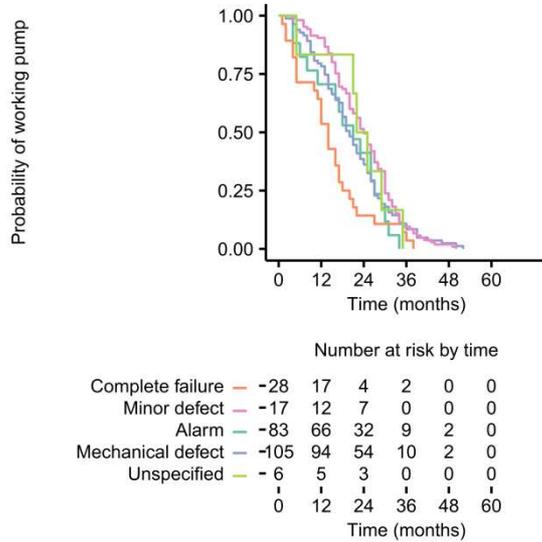
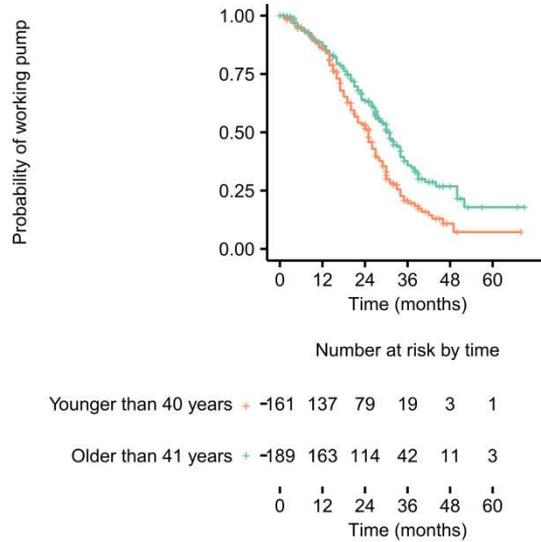


Fig. 1d - Survival according to age at pump initiation



ACCEPT

Pump brand	Total of pumps		Medtronic						Roche		Animas		p value	
			Paradigm®512/712		Paradigm®522/722		Paradigm®Veo™		Accucheck® Combo		20/20			
Pump model	n (%)	t [IQR] (months)	n (%)	t [IQR] (months)	n (%)	t [IQR] (months)	n (%)	t [IQR] (months)	n (%)	t [IQR] (months)	n (%)	t [IQR] (months)	n	t
Complete failure	28 (12)	13 [5-17]	4 (18)	10 [4-17]	8 (9)	10 [3-13]	6 (12)	16 [11-20]	3 (15)	34 [30-34]	7 (12)	12 [7-15]	0.72	0.89
Alarm	17 (7)	20 [11-27]	2 (9)	11 [7-14]	3 (4)	8 [6-14]	11 (21)	26 [19-28]	1 (5)	11 [11-11]	0 (0)	0 [0]	< 0.001	0.016
Total of severe failures	45 (19)	15 [8-23]	6 (27)	10 [4-17]	11 (13)	10 [3-13]	17 (33)	23 [16-28]	4 (20)	30 [23-34]	7 (12)	12 [7-15]	0.02	0.62
Mechanical defect	83 (35)	19 [13-26]	14 (64)	18 [11-26]	29 (34)	18 [10-28]	27 (53)	21 [14-25]	3 (15)	27 [14-34]	10 (17)	24 [18-27]	< 0.001	0.06
Minor defect	105 (44)	24 [16-30]	2 (9)	23 [19-28]	44 (51)	23 [16-30]	6 (12)	24 [14-27]	13 (65)	14 [11-16]	40 (66)	25 [21-30]	< 0.001	< 0.001
Total of not severe failures	188 (79)	21 [15-29]	16 (73)	18 [13-27]	73 (85)	21 [14-30]	33 (65)	21 [14-26]	16 (80)	14 [10-21]	50 (83)	25 [20-30]	0.02	0.003
Unspecified	6 (2)	23 [21-27]	0 (0)	0 [0]	2 (2)	30 [27-32]	1 (2)	28 [28-28]	0 (0)	0 [0]	3 (5)	21 [12-21]	0.78	0.36
Total of defects	239 (68)	21 [14-28]	22 (61)	17 [9-26]	86 (80)	19 [13-30]	51 (53)	21 [14-27]	20 (57)	15 [11-27]	60 (81)	24 [18-29]	< 0.001	0.048

Table 1: Number of pump defects (n) and time before defect (t) according to pump model and type of defect. P-values were calculated for each type of defect comparing pump models. Complete failures and alarms were considered as “severe failures”. Mechanical defects and minor defects were considered as “not severe failures”

Table 2. Univariate and multivariate Cox proportional analysis for failure-free survival (n = 390)

	Univariate analysis		Multivariate analysis	
	HR (95% CI)	P value	HR (95% CI)	P value
Brand (ref: Medtronic)				
<i>Roche</i>	0,93 (0,58 ; 1,42)	0,76	-	-
<i>Animas</i>	1,29 (0,96 ; 1,74)	0,093	-	-
Model (ref: Medtronic Paradigm 512/712)				
<i>Paradigm 522/722</i>	1,49 (0,93 ; 2,38)	0,097	1,21 (0,72 ; 2,01)	0,47
<i>Medtronic Veo</i>	1,00 (0,60 ; 1,66)	0,99	0,78 (0,44 ; 1,36)	0,38
<i>Roche Combo</i>	1,13 (0,62 ; 2,08)	0,68	0,77 (0,39 ; 1,48)	0,43
<i>Animas 20/20</i>	1,57 (0,96 ; 2,57)	0,07	1,18 (0,69 ; 2,02)	0,54
CSII treatment duration (months)	0,98 (0,97 ; 1,007)	0,24	1,00 (0,99 ; 1,00)	0,97
Gender (ref: male)				
<i>Female</i>	1,40 (1,06 ; 1,86)	0,018	1,22 (0,89 ; 1,66)	0,20
Age at diabetes diagnosis (ref: 0 to 15 years)				
<i>16 to 30 years</i>	0,76 (0,57 ; 1,02)	0,07	-	-
<i>31 to 45 years</i>	0,62 (0,41 ; 0,93)	0,02	-	-
<i>More than 46 years</i>	0,55 (0,29 ; 1,04)	0,06	-	-
Diabetes type (ref: type 2 or other)				
<i>Type 1</i>	0,92 (0,55 ; 1,56)	0,77	0,97 (0,50 ; 1,89)	0,94
Age at first pump (ref : more than 40 years)				
<i>0 to 40 years</i>	1,59 (1,23 ; 2,05)	0,0003	1,64 (1,19 ; 2,25)	0,002
Number of previous pump (ref: none)				
<i>1</i>	0,85 (0,64 ; 1,14)	0,28	0,98 (0,72 ; 1,32)	0,89
<i>2</i>	0,94 (0,60 ; 1,46)	0,78	1,00 (0,61 ; 1,64)	0,99
<i>3 or more</i>	0,97 (0,43 ; 2,2)	0,94	1,09 (0,47 ; 2,55)	0,84
Number of previous failure (ref: none)				
<i>1</i>	1,04 (0,76 ; 1,43)	0,80	-	-
<i>2 or more</i>	1,26 (0,74 ; 2,13)	0,39	-	-

Multivariate analysis was stratified according to centers where CSII was initiated.

Selection of variables for multivariate analysis was done a priori without any specific automatic selection procedure. Brand, Age at diabetes diagnosis and number of previous failure were not included in the multivariate analysis due to collinearities with respectively Models, Age at first pump and number of previous pump.