Catheter Survival During Long-Term Insulin Therapy With an Implanted Programmable Pump

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OBJECTIVE — To survey catheter complications and to analyze catheter survival during long-term intraperitoneal and intravenous insulin therapy with an implanted programmable pump with a sideport.

RESEARCH DESIGN AND METHODS — Catheter occlusions were documented by measuring dynamic catheter resistance. Catheter migrations or breaks were demonstrated by X ray. When flushing the catheter with buffer solution through the sideport failed to clear the occlusion, catheters were replaced or laparoscopy was performed for the excision of fibrous tissue growth. Broken or migrated catheters were replaced.

RESULTS — Occlusions were the most common catheter complications, and the majority of them (79% intraperitoneal and 84% intravenous) were cleared by flushing the catheter. Survival at 3 years was significantly higher for intraperitoneal catheters compared with intravenous catheters (60% intraperitoneal and 22% intravenous).

CONCLUSIONS — Nonsurgical management of catheter occlusions contributed to extend catheter lifetime. Intraperitoneal catheters have a lower morbidity and a higher survival than intravenous catheters.

During insulin therapy using an implanted pump, catheter complications are observed with both intraperitoneal and intravenous delivery (1–7). Occlusions, caused by deposition of insulin aggregates inside the lumen and by fibrous tissue growth or clotting at the tip and inside the distal end, are the most frequent catheter complications (8–11). Migrations, breaks, and, for intravenous catheters, venous thrombosis are less common (1).

Since noninvasive diagnosis of catheter occlusions was impossible in earlier models of implantable insulin pumps, previous surveys of catheter complications were based on visual inspection of the catheter during laparoscopy or on examination of the explanted catheter (1,8,9,11). In implantable devices with sideports (i.e., a direct access to the insulin path between the outlet valve of the pumping unit and the catheter hub) (2,5,6), catheter patency can be documented by measuring catheter resistance by a minimally invasive procedure (12). Furthermore, flushing the catheter with buffer solution through the sideport can be attempted to clear occlusions (12).

We report a survey of all catheter complications and catheter survival analysis during long-term intraperitoneal and intravenous insulin delivery using an implanted programmable pump with a sideport.

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NF, normalized flow; $T_{1/2}$, time for sideport pressure to decrease by 50%.

RESEARCH DESIGN AND METHODS

— The description of the Infusaid Model 1000 pump (Strato/Infusaid, Norwood, MA) and the results of the clinical trial in patients with type I diabetes are reported elsewhere (2,5). The device is implanted in a subcutaneous pocket created within the abdominal wall and attached to the fascia. The distal portion (10 cm) of the intraperitoneal catheter is inserted in the peritoneal cavity through a 1- to 2-cm transmuscular incision in the pocket area. The intravenous catheter is tunneled subcutaneously in the lateral abdomen and then inserted in the left subclavian vein. Both intraperitoneal and intravenous catheters are secured by suturing the catheter flange to the fascia. Volume flow performance of the pump is expressed by normalized flow (NF), i.e., the ratio between the volume of insulin infused (actual infused volume) divided by the volume of insulin programmed to be delivered (expected infused volume). The NF is calculated at each refill of the pump reservoir and is a function of pumping unit performance and catheter patency.

Our catheter database includes 117 patients followed at 16 centers (9 in the U.S. and 7 in Europe) since 1989. Patients received pump insulin therapy through the intraperitoneal route ($n = 91$, 273.9 patient-years, range 0.3–3.7 years) or through the intravenous route ($n = 26$, 38.8 patient-years, range 0.1–3.6). Seventeen patients receiving intravenous insulin treatment were changed to the intraperitoneal route because of complications with the intravenous catheter. Catheter complications were documented according to the following protocol: When NF <0.9, deterioration in metabolic control, or increase in daily insulin need were observed, then *1*) patency of the catheter lumen was determined by measuring dynamic catheter resistance (i.e., the time for sideport pressure to decrease by 50% [$T_{1/2}$] after injection of 0.1 ml of buffer solution), and 2) performance of the pumping unit was assessed by directly measuring pump outflow at the sideport (12). In case of increased catheter resistance ($T_{1/2} > 10$ s), flushing the catheter with buffer solution through the sideport was attempted to clear

Table 1—*Catheter complications during long-term insulin pump therapy in IDDM patients*

	Intraperitoneal	Intravenous
Occlusions (events/patients)	157/70	49/18
Resolved by flushing (reversible)	124 (79)	41 (84)
Requiring surgery (irreversible)	33 (21)	8 (16)
Time to 1st event (months/events)	16.1 ± 10.3/70	8.9 ± 6.5/18
Time to 2nd event (months/events)	5.9 ± 6.3/37	6.0 ± 8.2/14
Time to 3rd event (months/events)	6.5 ± 7.1/24	3.4 ± 3.7/8
Time to 4th event (months/events)	6.5 ± 7.1/24	4.9 ± 4.2/5
Migrations (events/patients)	4/4 (3.7)	6/5 (19.2)
Breaks (events/patients)	9/9 (9.9)	2/2 (7.7)
Venous thrombosis (events/patients)	NA	4/3 (11.5)

Data are *n*, *n* (%), or means ± SD In the intraperitoneal catheter group, seven patients had five occlusions, three patients had six occlusions, and two patients had seven occlusions. In the intravenous catheter group, three patients had five occlusions and one patient had six occlusions. NA, not applicable.

the occlusion. The finding of a patent catheter in patients with normal NF and inadequate metabolic control prompted evaluation of catheter position and integrity by X ray, with or without contrast media.

The first intraperitoneal and the first intravenous catheters implanted in a patient were considered for survival analysis, i.e., 108 intraperitoneal catheters (cumulative intraperitoneal catheter life 228.7 years, range 0.2–3.7 years) and 26 intravenous catheters (cumulative intravenous catheter life 36.0 years, range 0.1–3.6 years). Survival function was calculated according to the product-limit or Kaplan-Meier method (13), considering end-of-catheter-life events (e.g., irreversible occlusions, breakage at the catheter hub, or catheter migrations) requiring surgical intervention for management or replacement. Catheters explanted with a patent lumen because of pumping unit complications or patient choice (13 intraperitoneal and 2 intravenous) were considered to be lost to follow-up. The difference between the survival functions of intraperitoneal and intravenous catheters was tested using a nonparametric linear-rank test (Mendel-Cox statistic) (14).

RESULTS — Catheter complications documented during this study are summarized in Table 1. The majority of occlusions (79% intraperitoneal and 84% intravenous) were resolved by flushing the catheter with buffer solution through the sideport. Of the 33 intraperitoneal occlusions requiring surgery, 27 occurred in the first implanted catheter and 6 in the replacement catheters, with rates of surgery of 0.12 and 0.13 events per patient-year, respectively. Eight occlusions requiring surgery occurred in intravenous catheters (rate of surgery, 0.20 events per patient-year), and in seven cases, the intravenous catheter was replaced with an intraperitoneal catheter. Repeated occlusions occurred in both intraperitoneally and intravenously treated patients. During intraperitoneal insulin treatment, 14 patients (20% of the patients with occlusions) had four or more occlusions, accounting for 43% of the occlusions of intraperitoneal catheters. Five patients (28% of the patients with occlusions) had four or more occlusions during intravenous insulin treatment, accounting for 49% of the intravenous occlusions. Migrations and hub breaks required surgical intervention for catheter replacement, with the exception of one migrated intravenous catheter, which was resutured in place. Four events of venous thrombosis occurred in intravenous catheters: three required removal of the catheter and one was resolved with thrombolytic therapy.

Probability of catheter survival without surgery (all causes) after 1, 2, and 3 years of insulin delivery was 89 ± 3.1, 74 ± 4.3, and 60 ± 5.7% for intraperitoneal catheters (Fig. 1*A*) and 68 ± 10.1, 41 ± 11.2, and 22 ± 10.2% for intravenous catheters (Fig. 1*B*) ($P < 0.0004$, intraperitoneal versus intravenous). Occlusions were the primary cause of surgical intervention in both intraperitoneal and intravenous catheters, and survival of intravenous catheters was significantly shorter compared with intraperitoneal catheters ($P < 0.007$). Migrations also contributed to decreased

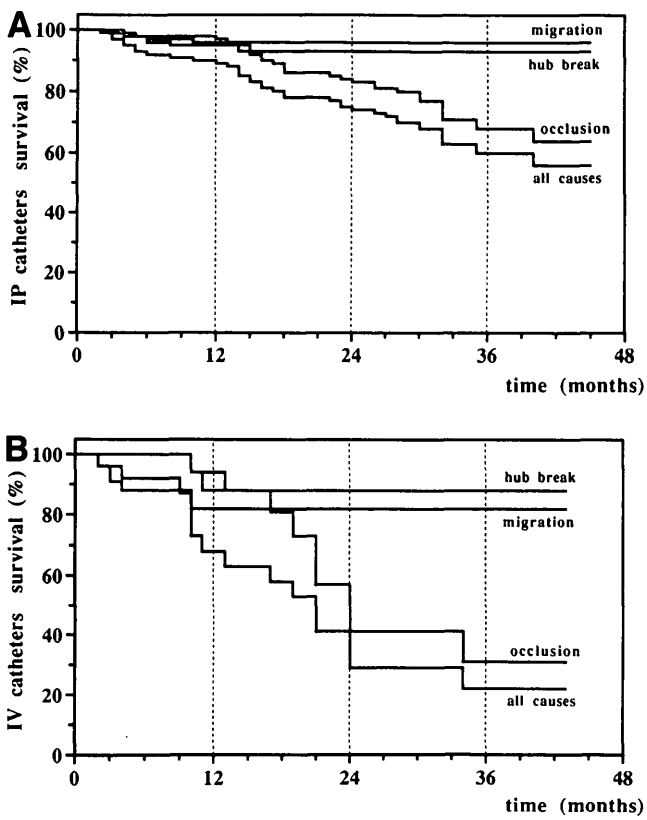

Figure 1—*Survival curves of intraperitoneal (A) and intravenous (B) catheters during long-term insulin pump therapy in IDDM patients.*

survival of intravenous catheters compared with intraperitoneal catheters ($P < 0.02$), while no significant difference in survival was observed because of hub breaks.

CONCLUSIONS — In our survey, occlusions were the most frequently documented complication in both intraperitoneal and intravenous catheters. The majority of occlusions (79% intraperitoneal and 84% intravenous) were resolved by a simple nonsurgical procedure, i.e., flushing the catheter with buffer solution injected through the sideport. Reversible catheter occlusions have never been reported before, because in implantable insulin pumps without a sideport, no diagnostic option was available and no management was possible in case of suspected catheter occlusion except surgical replacement or clearing of the tip during laparoscopy. Because in this study we attempted to clear all documented occlusions by flushing before considering surgery, we do not know the proportion of the occlusions reversed by flushing that would have evolved into occlusions requiring surgery for resolution. However, our rate of surgery for the replacement of intraperitoneal catheters is one of the lowest reported in the literature (6–9,11), and our 3-year survival of intraperitoneal catheters is twofold higher than that reported when using laparoscopy to assess catheter status in cases of suspected occlusion (11); this is possibly because in our study, catheter occlusions were cleared at an early stage by flushing.

In both intraperitoneal and intravenous catheters, repeated catheter occlusions occurred in a relatively small subset of patients (20 and 28% of the patients with intraperitoneal and intravenous occlusions, respectively), suggesting that individual patients may be predisposed to occlusions, as was observed in external pumps for intraperitoneal insulin delivery (10).

Catheter breaks at the hub were eliminated when the manufacturer improved the design of the hub connection. Migrations were an early event in catheter life and were decreased by improving the surgical technique for catheter fixation.

The present data extend our previous observation (2) that survival of catheters for insulin delivery is significantly longer for the intraperitoneal route compared with the intravenous route because of the higher rate of irreversible occlusions and migrations and the occurrence of venous thrombosis. The lower morbidity of intraperitoneal catheters accounts for the predominant choice of this route of insulin delivery for pump insulin therapy (1).

In conclusion, catheter occlusions are the most common catheter complication during pump insulin therapy. Flushing the catheter with buffer solution through the sideport contributed to extend catheter lifetime. Intravenous catheters have a shorter survival than intraperitoneal catheters because of a higher rate of occlusions, migrations, and the occurrence of venous thrombosis.

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APPENDIX

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