Development of a Simplified Method to Measure Intra-abdominal Pressure in Peritoneal Dialysis Patients

Investigators:

Deb Zimmerman (Nephrology, PI)
Brian Blew (Urology, co-investigator)
Daniel Corsi (Methods Centre Statistician, co-investigator)
Hilary Meggison (Intensive Care, co-investigator)
Jeff Warren (Urology, co-investigator)
Tharshika Thangarasa (Medical Student, University of Ottawa)

Pilot Study, 1 year

NCT02811640

ABSTRACT

BACKGROUND: Patients treated with peritoneal dialysis (PD) are at increased risk to develop mechanical complications such as dialysate leaks and hernias thought to be related to an increase in intra-abdominal pressure (IAP) secondary to the addition of dialysate to the abdomen. Resistance training has been shown to increase IAP but it is unclear in the general population and in patients treated with PD if this training increases the risk of developing hernias.

AIMS/HYPOTHESES: We therefore propose this pilot study in which our specific aim is to: 1) Observe the difference in IAP pressure measurements that are obtained using the simple hand held Stryker pressure monitor via the PD catheter compared to the standard IAP measurements obtained with the insufflator at the time of PD catheter insertion. This tool will then be used as part of a future larger trial in which we will: 1) Measure IAP with resistance training in patients treated with PD; with and without dialysate, 2) Assess PD patient interest in participating in resistance training trials, and 3) Determine the appropriateness of the proposed resistance training program for this patient population. Our ultimate goal is to develop a randomized clinical trial to: 1) assess the impact of resistance training on quality of life and functional status, 2) assess the risk of developing leaks/hernias, and 3) determine if there is an association between IAP during resistance training and subsequent hernia development.

RESEARCH PLAN:
Ten patients who are having a PD catheter inserted in the operating room and provide informed consent will undergo IAP measurements with the Stryker pressure monitor. Values will be compared to the insufflator at inflation pressures of 5, 10, and 15 mmHg. Bland Altman plots will be constructed and considered acceptable if the mean difference between the readings is 5mmHg and 95% of the points fall within 2 standard deviations of the mean difference. If the Stryker pressure monitor is not found to be appropriate for measuring IAP in PD patients, more complicated methods that have been used historically will be validated if necessary.

IMPACT: After the initiation of dialysis, functional status declines. Sedentary life-style and low muscle strength are important predictors of mortality for patients treated with dialysis. Yet patients treated with PD are advised not to participate in resistance training programs for fear of hernia development. Ultimately, our research program has the potential to help many patients with end stage kidney disease to remain active if we are able to define the risks and benefits of an appropriately designed resistance training program.

1.1 Overview
Patients with end stage kidney disease (ESKD) are at increased risk to develop functional impairment after the initiation of dialysis. Resistance training has been shown to improve muscle strength and self-esteem in other chronic diseases but has been not been studied in patients with ESKD treated with peritoneal dialysis (PD). The reasons for this may be multifactorial but almost certainly include concerns about increasing the risk for developing hernias.

1.2 Hypothesis and Long Term Objectives
Hypothesis: The observed intra-abdominal pressure (IAP) as assessed by the Stryker pressure monitor via the PD catheter will be similar to the IAP measured by the insufflator at the time of PD catheter insertion. If this hypothesis is correct, we will develop a future resistance training program for PD patients as part of a randomized clinical trial to: 1) assess the impact of resistance training on quality of life and functional status, 2) assess the risk of developing leaks/hernias, and 3) determine if there is an association between IAP during resistance training and subsequent hernia development.

1.3 Background Rationale: Current state of knowledge

1.3.1 Risk of Hernias in the General Population
A hernia is a general term referring to a protrusion of a tissue through the wall of the cavity in which it is normally contained. In the First National Health and Nutrition Examination Survey, 13.9% of men and 2.1% of women developed an inguinal hernia after a median follow-up of 18.2 years.[1] For men and women, inguinal hernias were associated with increased age and history of other hernias. In a separate case-control study of 1418 male patients with inguinal hernias, only a positive family history of inguinal hernias was important.[2] The importance of weight lifting/resistance training as a cause of hernias was not addressed in any of the studies.

1.3.2 Risk of Hernias for Patients with End Stage Kidney Disease Treated with Peritoneal Dialysis
Patients treated with PD may develop dialysate fluid leaks especially around the site of the peritoneal dialysis catheter and/or hernias typical of the general population. In one small study of 142 patients treated with PD over 5 years, 53 patients developed either a leak or hernia.[3] The independent risk factors for peri-catheter leak and hernias were higher body mass index and polycystic kidney disease respectively. Importantly, the percentage of patients with hernias prior to starting PD was not reported. The majority of hernias develop early after the initiation of PD raising the possibility of pre-existing abdominal wall defects that become obvious with the increase in intra-abdominal pressure associated with PD.[4,5] In a study of 122 patients, 19 hernias were detected in 15 patients prior to starting PD; 7 new hernias were detected during an average follow-up of 2 years after starting PD.[6] The authors did not discuss if the hernias pre/post dialysis were in the same patients. In a more recent study, the only statistically significant risk factor for developing a hernia after starting PD was the occurrence of a hernia prior to dialysis ($p=0.01$).[7] History of lifting was not assessed in any of the studies. Despite a lack of compelling evidence, patients treated with PD are advised not to participate in heavy lifting in order to reduce the risk of increased intra-abdominal pressure with activity.[8-11]

1.3.3 Methods to Measure IAP
Methods to measure IAP have been developed for very diverse reasons including monitoring for the development of intra-abdominal compartment syndrome. Patients at high risk for development of the syndrome are monitored approximately every 8 hours via bladder pressure measurements. This technique was originally described by Iberti et al in 1989.[12] The investigators described a comparison of IAP measured directly via paracentesis or through a

Jackson Pratt drain to values obtained via a foley catheter. The 2 methods of IAP measurement were highly correlated (r=0.91). Two other groups of investigators have compared direct IAP measurements using different techniques to those obtained from the insufflator during surgery.[13,14] In one study, the comparator was a round PVC drain connected to an arterial blood pressure set. The correlation between the two measurements was excellent (0.97).[13] In the second study, direct pressure measurement using the Stryker intracompartmental pressure monitor was described.[14] The system used in the study consisted of a monitor (STIC), a sterile disposable indwelling slit catheter set with extension tubing and an introducing needle that is attached to the continuously reading monitor. The pressure measurements obtained by the STIC monitor correlated very well with the pressure measurements of the insufflator used during laparoscopic surgery with a mean difference between the 2 techniques of 0.04 ± 3.8mmHg.

Very few studies actually report IAP measurements in patients treated with PD. In the first study, IAP was assessed using a CVP monometer connected to an outflow line and estimated at the level of the umbilicus in supine position.[15] IAP increased from 0.37 to 1.10mmHg in a linear fashion with increasing volumes of dialysate. In 1983 using a similar measurement technique, Twardowski and colleagues estimated IAP with a CVP manometer connected to the dialysis catheter from the level of the umbilicus in the supine position and xiphoid process in the sitting and standing positions.[16] They demonstrated: 1) an increase in IAP with increasing volumes of dialysate, and 2) IAP was influenced by position. After modifying their technique to include continuous monitoring with a pressure transducer connected to the PD catheter via a 3 way stop cock, this same group of investigators measured IAP with 'normal' activity including jogging, cycling, jumping, lifting (0, 11.4 and 22.8kgs), coughing and straining with dialysate volumes increasing from 0 to 3L.[17] Coughing and straining were associated with the greatest IAP with pressures as high as 230mmHg recorded (Figure 1). IAP increased with increasing weight lifted to a maximum of about 100mmHg with little difference between the different dialysate volumes with weights lifted of 11.4 and 22.8kgs. Using a slightly different technique in which IAP was estimated at the centre of abdomen in the mid-axillary line, no difference in 'resting' pressures was detected between patients with and without mechanical complications such as hernias.[18] This was not true for children in which those with mechanical complications had a slightly higher resting IAP.[19]

1.3.4 Patients with End Stage Kidney Disease and Loss of Functional Status

After the initiation of dialysis, functional status declines. In a study of nursing home residents, the Minimum Data Set–Activities of Daily Living scale increased from 12 in the 3 months prior to starting dialysis to 16 during the 3 months after starting dialysis with higher numbers reflecting greater functional difficulty.[20] At 12 months post dialysis initiation, 58% of the patients had died and only 13% had maintained their pre-dialysis functional status. Of elderly patients already on dialysis, approximately 50% require assistance with personal care which is compounded by losses of muscle strength during periods of hospitalization.[21] In a nutritional study of patients treated with CAPD, women were found to have significant weight loss related to muscle wasting.[22] Importantly, sedentary life-style and low muscle strength are important predictors of mortality for patients treated with dialysis.[23-26]

1.3.5 Benefits of Resistance Training in Patients with Chronic Diseases

The supervised trial of aerobic versus resistance training was the first study in women with breast cancer being treated with chemotherapy.[27] Resistance training was found to increase self-esteem, muscular strength and lean body mass. In a recent meta-analysis of cancer survivors, resistance training of low to moderate intensity was associated with clinically important effects on muscle function and body composition.[28]Resistance training has also been shown to be of benefit with respect to muscle strength in men with chronic obstructive pulmonary disease, patients with congestive heart failure and may be the training modality of choice in the frail elderly for the maintenance of activities of daily living.[29-31] Additional benefits of resistance training include improved glycemic control, blood pressure and serum triglyceride levels which may offer additional cardiovascular benefits to patients treated with peritoneal dialysis.[31]

In hemodialysis, a few small studies have examined the impact of resistance training on a variety of outcomes. In a 12-week intra-dialytic resistance training program for 10 hemodialysis patients, there was a statistically significant improvement in the performance of the 6 minute walk test, normal and maximal gait speed and time to complete a sit-stand test 10 times.[32] Muscle strength has also been shown to increase with resistance training in patients treated with hemodialysis.[33-35] To our knowledge, there haven't been any studies of resistance training in peritoneal dialysis patients. It is unclear if this is secondary to: 1) more difficult patient population to study than patients treated with hemodialysis, or 2) concerns about mechanical complications such as hernias in the peritoneal dialysis population.

Summary of the Available Evidence

Patients treated with peritoneal dialysis are at increased risk to develop mechanical complications such as dialysate leaks and hernias thought to be related to an increase in IAP secondary to dialysate. Weight lifting has been shown to increase IAP but it is unclear in the general population and in patients treated with peritoneal dialysis if resistance training actually increases the risk of developing hernias. However, it is clear that there are physical and psychological benefits associated with resistance training that may be of particular importance to patients treated with peritoneal dialysis. Currently IAP is not measured routinely in PD patients except at the time of catheter insertion and there is not an accepted 'standard' way to measure IAP for research in PD patients. We therefore propose this study in which we will develop an easy to use method to measure IAP in patients treated with PD such that this technique could be easily applied in future clinical care and research studies.

SECTION 2: TRIAL DESIGN

2.1 Inclusion Criteria

Adult patients (≥18 years old) with chronic kidney disease that will have a PD catheter inserted in the operating room at the Ottawa Hospital using laparoscopic surgery. Able and willing to give informed consent.

2.2 Exclusion Criteria

Patients who will have a non-standard PD catheter insertion position (eg parasternal)

2.3 Study Protocol

Basic demographic information will be collected including: age, sex, height, weight, comorbid illnesses and cause of kidney failure.

Development of a Simple IAP measurement technique

The Stryker intracompartmental monitor is a simple to use, hand-held, portable device that would make it ideal for a multicentre study in which IAP could be measured in a large number of patients in diverse research/clinic environments. The pressure monitor system was developed to detect compartment syndrome and includes a small pressure monitor and a sterile fluid path that includes a side-ported needle (https://www.stryker.com/en-us/products/SurgicalEquipment/PressureMonitors/IntraCompartmentalPressureMonitor/index.htm). For our purposes, the pressure system (without the side port needle) would be directly connected to the PD catheter via sterile extension tubing as described below (Figure 2).

Standard cannulation of the abdomen by the surgeon will be undertaken followed by insufflation, insertion of trochars as required and placement of the internal portion of the PD catheter in the true pelvis. The PD catheter will be flushed with normal saline or lactated ringers. Then the external portion of the catheter will be connected to the Stryker monitor using sterile extension tubing. With the patient at end-expiration (typical of lifting), the pressure measured from the PD catheter at the level of the umbilicus in the mid-axillary line will be compared to the insufflator at 15, 10 and 5mmHg. If the easy to use Stryker pressure monitor is found to be inappropriate for our purpose (see data analysis), the standard IAP measurement that has been developed for foley catheters and modified for PD catheters in the past will be used. Briefly, the PD catheter will be flushed with normal saline or lactated ringers as above and connected to a transfer set and TEGO® adapter. The TEGO® will then be connected to arterial tubing, a pressure transducer and a pressure monitor (present in the operating room). This is the same type of set up that is used in the intensive care unit with the exception that the pressure transducer and arterial tubing are connected to the sampling port of the foley catheter. With the patient at end-expiration, the pressure measured from the PD catheter zeroed at the level of the umbilicus in the mid-axillary line will be compared to the insufflator at 15, 10 and 5mmHg.

2.5 Sample Size and Analysis

Summary descriptive statistics to describe the patient population will be calculated. The proportion of screened patients that are: 1) eligible, and 2) agree to participate will be determined. We will recruit 12 participants. Bland Altman plots will be constructed and considered acceptable if the mean difference between the readings is 5mmHg and 95% of the points fall within 2 standard deviations of the mean difference. Based on previous literature, correlation coefficients will also be assessed and considered acceptable if the calculated value is greater than 0.9. If these targets are not met, the first phase will be repeated using the arterial tubing, pressure transducer and pressure monitor as has been used historically.

2.6 Time Lines and Feasibility

Last year, Drs Warren and Blew inserted 123 PD catheters laparoscopically; 49 of these catheters were left exteriorized and would have had transfer sets connected to them. Typically there are 2 surgical days/month with about 5 patients per day. The time needed to do the IAP measurements is very small and will not affect OR flow such that up to 5 patients could be tested in a single OR day. Allowing for time for REB approval, recruitment of patients and data-analysis – the study is anticipated to take approximately one year.

2.7 The Research Team

Dr Zimmerman is a nephrologist at the Ottawa Hospital and a clinician investigator with the KRC and OHRI. She has a MSc in clinical epidemiology and extensive clinical research experience. Dr Meggison is an intensivist at the Ottawa Hospital and has experience with the measurement of intra-abdominal pressure. She will provide clinical expertise and assistance with intra-abdominal pressure monitoring. Drs Jeff Warren and Brian Blew are urologists at the Ottawa Hospital. They are responsible for insertion of all of the PD catheters for the Ottawa Hospital Home Dialysis Program. They will assist in the coordination of PD catheter insertion and IAP measurements. Dr Dan Corsi has a PhD in Epidemiology and Population Health from McMaster University. He is a statistician with the Methods Centre of the Ottawa Hospital Research Institute. He was responsible for our sample size calculations and he will oversee all statistical analysis at the completion of the study. Tharshika Thangarasa is a medical student with funding support from the University of Ottawa; this will serve as her summer project.

REFERENCES

1. Ruhl CE, Everhart JE. Risk factors for inguinal hernia among adults in the US population. Am J Epidemiology 2007; 165(10): 1154-1161
2. Lau H, Fang C, Yuen WK, Patil NG. Risk factors for inguinal hernia in adult males: a case-control study. Surgery 2007; 141(2): 262-266
3. Del Peso G, Bajo MA, Costero O, Hevia C, Gil F, Diaz C, Aguilera A, Selgas R. Risk factors for abdominal wall complications in peritoneal dialysis patients. Perit Dial Int 2003; 23: 249-254
4. Tsang LY, Hung CY, Peng SJ, Ferng SH, Yang CS. Hernia in ESRD patients receiving peritoneal dialysis 2002. Acta Nephrologica 2002; 16: 57-61
5. LeBlanc M, Oulmet D, Pichette V. Dialysate leaks in peritoneal dialysis. Seminars in Dialysis 2001; 14(1): 50-54
6. García-Ureña MA, Rogriguez CR, Ruiz VV, Hernandez FJC, Fernandez-Ruiz E, Gallego JMV, Garcia MV. Prevalence and management of hernias in peritoneal dialysis patients Perit Dial Int 2006; 26: 198-2002
7. Toledo MG, Sans MB, Gabarrell A, Durain J, Giraldez EF. Risk factors for abdominal hernias in patients undergoing peritoneal dialysis Nephrologia 2011; 31(2): 218-219
8. Bargman J. Hernias in peritoneal dialysis patients: limiting occurrence and reoccurrence. Perit Dial Int 2008; 28: 349-351
9. http://www.homedialysis.org/life-at-home/articles/hernias-and-peritoneal-dialysis; July 21, 2015
10. http://www.davita.com/treatment-options/home-peritoneal-dialysis/what-is-peritoneal-disease-/peritoneal-dialysis:-your-first-year/t/5485; July 22, 2015,
11. http://www.renalnetwork.on.ca/common/pages/UserFile.aspx?fileId=257562, July 22, 2015
12. Iberti TJ, Lieber CE, Benjamin E. Determination of Intra-abdominal pressure using a transurethral bladder catheter: clinical validation of the technique. Anesthesiology 1989; 70: 47-50
13. Risin E, Kessel B, Lieberman N, Schmilovich M, Ashkenazi I, Alfici R. New technique of direct intra-abdominal pressure measurement. Asian J Surg 2006; 29(4): 247-250
14. Brooks AJ, Simpson A, Delbridge M, Beckingham IJ, Girling KJ. Validation of direct intraabdominal pressure measurement using a continuous indwelling compartment pressure monitor. Journal of Trauma, Injury, Infection and Critical Care 2005; 58: 830-832
15. Gotloib L, Mines M, Garmizo L, Varka I. Hemodynamic effects of increasing intraabdominal pressure in peritoneal dialysis. Perit Dial Int 1981; 1(4): 41-43
16. Twardowski ZJ, Prowant BF, Nolph KD, Marinez AJ, Lampton LM. High volume, low frequency continuous peritoneal dialysis. Kidney Int 1983; 23: 64-70
17. Twardowski ZJ, Khanna R, Noph KD, Scalamogna A, Metzler MH, Schneider TW, Prowant BF, Ryan LP. Intraabdominal pressures during natural activities in patients treated with continuous ambulatory peritoneal dialysis. Nephron 1986; 44: 129-135

18. Durand FY, Chauliau J, Gamberoni J, Hestin D, Kessler M. Routine measurement of hydrostatic intraperitoneal pressure. Adv Perit Dial 1992; 8: 108-112
19. Aranda RA, Romao Junior JE, Kakehashi E, Domingos W, Sabbaga E. Intraperitoneal pressure and hernias in children on peritoneal dialysis. Ped Nephrol 2000; 14: 22-24
20. Tamura MK, Covinsky KE, Chertow GM, Yaffe K, Landefield CS, McCulloch CE. Functional status of elderly adults before and after initiation of dialysis. New Engl J Med 2009; 361: 1539-1547
21. Jassal SV, Watson D. Dialysis in late life: benefit or burden. Clinical J Am Soc Nephrol 2009, 4: 2008-2012
22. Young GA, Lopple JD, Lindholm B, et al. Nutritional assessment of continuous ambulatory peritoneal dialysis patients: an international study. Am J Kidney Dis 1991; 17(4): 462-471
23. McClellan WM, Anson C, Birkeli K, Tuttle E. Functional status and quality of life: predictors of early mortality among patients entering treatment for end stage renal disease J of Epidemiology 1991; 44(1): 83-89
24. Johansen KH. Exercise in end-stage renal disease population. J Am Soc Nephrol 2007; 18: 1845-1854
25. Lopes AA, Lantz B, Morgenstern H et al. Associations of self-reported physical activity types and levels with quality of life, depressive symptoms, and mortality in hemodialysis patients. Clin J Am Soc Nephrol 2014; 9 (10): 1702-1712
26. Isoyama N, Qureshi AR, Avesani CM et al. Comparative associations of muscle mass and muscle strength with mortality in dialysis patients. Clin J Am Soc Nephrol 2014; 9 (10): 1720-1728
27. Courneya KS, Segal RJ, Mackey JR et al. Effects of aerobic and resistance exercise in breast cancer pateitns receiving adjuvant chemotherapy : a multicenter randomized controlled trial. J. Clin. Onc. 2007; 25 :4396-4404
28. Strasser B, Steindorf, Wiskemann, Ulrich C M. Impact of resistance training in cancer survivors : a meta-analysis. Med Sci Sports Exerc. 2013;45(11):2080-2090).
29. Casaburi R, Bhasin S, Cosentino L, et al. Effects of testosterone and resistance training in men with chronic obstructive pulmonary disease. Am J Respir Crit Care Med 2004; 170: 870-878
30. Pu CT, Johnson MT, Forman DE et al. Randomized trial of progressive resistance training to counteract the myopathy of chronic heart failure. J Appl Physiol 2001; 90(6): 2341-2350
31. Hurley BF, Hanson ED, Sheaff AK. Strength training as a countermeasure to aging muscle and chronic disease. Sports Med 2011;41(4):289-306)
32. Headley S, Germain M, Mailloux J et al. Resistance training improves strength and functional measures in patients with end-stage renal disease. Am J Kid Dis 2002; 40(2): 355-364
33. Cheema B, Abas H, Smith B, O'Sullivan A, Chan M, Patwardhan A, Kelly J, Gillin A, Pang G, Lloyd B, Singh MF. Randomized controlled trial of intradialytic resistance training for

target muscle wasting in ESRD: the progressive exercise for anabolism in kidney disease (PEAK) study. Am J Kid Dis 2007; 50: 574-584
34. Johansen KL, Painter PL, Sakkas GK, Gordon P, Doyle J, Shubert T. Effects of resistance exercise training and nandrolone decanoate on body composition and muscle function among patients who receive hemodialysis: A randomized, controlled trial. J Am Soc Nephrol 2006; 2307-2314
35. Heiwe S, Jacobson SH. Exercise training for adults with chronic kidney disease. Cochrane Database Syst Rev (10): CD003236, 2011

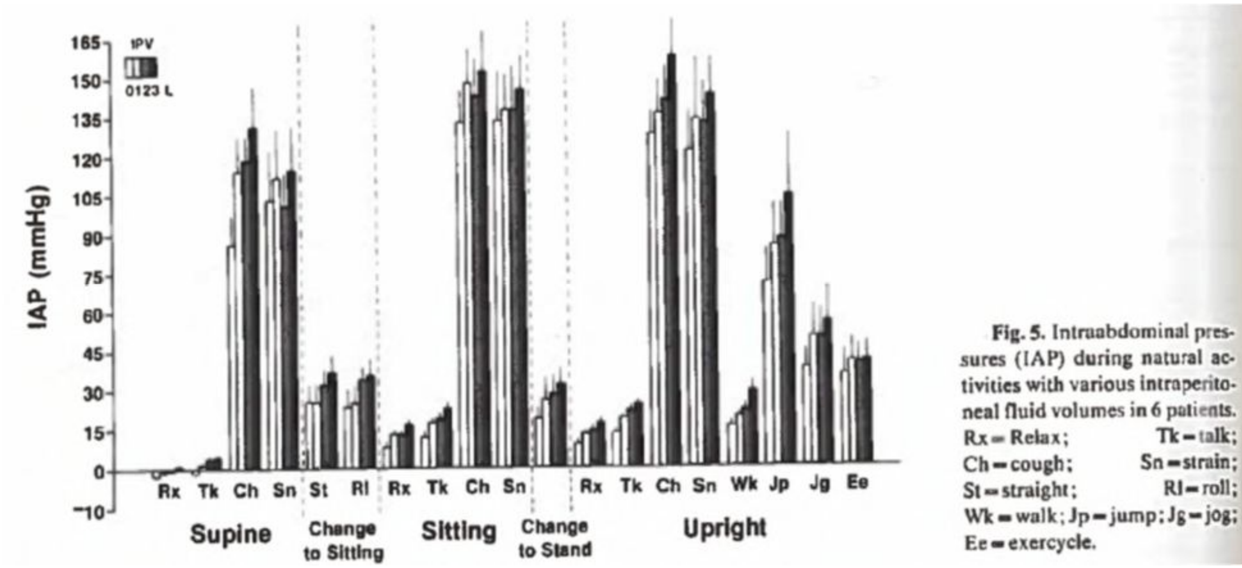

Figure 1: Intra-abdominal pressure in PD patients with different activities

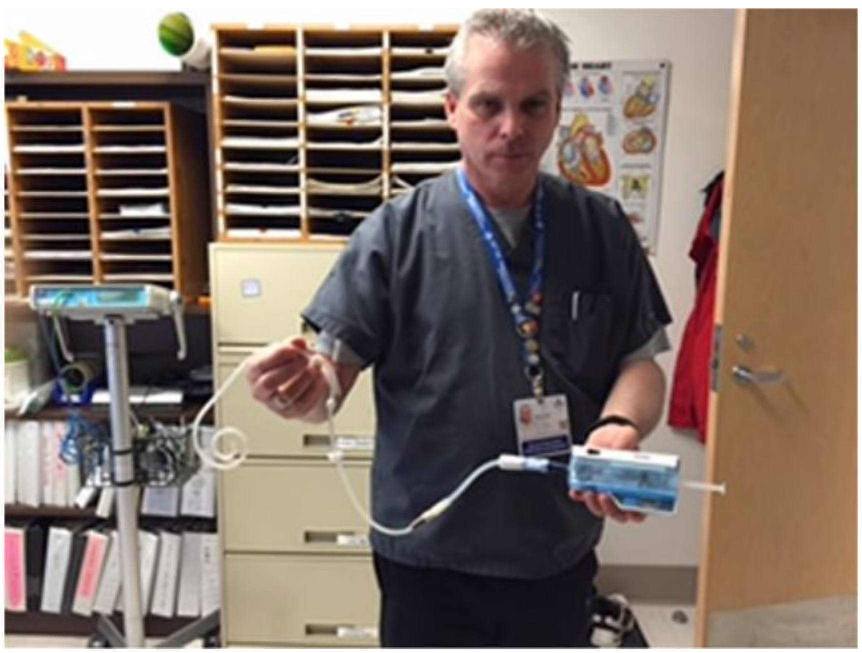

Figure 2: Stryker Pressure Monitor Connected to a PD catheter