Prognostic Role of Arterial Stiffness in Peritoneal Dialysis Patients

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Arterial stiffness, defined as a decreased ability of the conductive arteries to absorb the pulse pressure has been reported to be a strong independent predictor of overall cardiovascular mortality in the general population and chronic kidney disease (CKD). Carotid-femoral pulse wave velocity (CF-PWV) has been used in the epidemiological studies demonstrating the predictive value of aortic stiffness for cardiovascular events [1] and has been widely proved to be associated with many cardiovascular risk factors in PD patients[2,3]. Although the CF-PWV is used as the “gold standard” for measuring aortic stiffness, some recently studies indicated that PWV ratio (carotid-femoral pulse wave velocity divided by carotid-radial pulse wave velocity) could be a better indicator than CF-PWV [4,5].

The PWV ratio is a relatively new concept in arterial research. Under physiological conditions, the arterial vasculature is characterized by a progressive increase in stiffness from the aorta and large elastic arteries toward the peripheral muscular conduit arteries, often labeled as the arterial stiffness gradient [6]. This reversal of the normal arterial stiffness gradient, named stiffness mismatch assessed by PWV ratio, enhance the transmission of pulsatile energy into the periphery and microcirculation and, theoretically, increase the risk for damage to microvascular beds in highly perfused organs [4,6]. Fortier et al demonstrated that PWV ratio was a better prognostic predictor of all-cause mortality than CF-PWV per se in a prevalent dialysis cohort with a median follow-up of 29 months [5]. However, findings from a recent study do not support the notion that PWV ratio provides additional prognostic value over conventional CF-PWV in the community [7]. Thus, the prognostic value of PWV ratio need to be
confirmed. It should be noted that the study from Fortier included only 65 (21%) PD patients. Given that different dialysis modality may have distinct impact on arterial stiffness, possible predictive value of aortic-brachial arterial stiffness mismatch assessed by PWV ratio in PD patients' outcomes need to be further elucidated.

To investigate the prognostic value of aortic-brachial stiffness mismatch assessed by PWV ratio on PD patients, we recently performed analysis of PWV from a longitudinal cohort including 181 incident PD patients who started PD during September 20, 2005, to February 05, 2008 with patients' both all-cause and cardiovascular (CVD) mortality were analysis as of January 31, 2018 [8]. Aortic-brachial arterial stiffness mismatch was assessed using PWV ratio. Results showed that median survival of patients in PWV ratio above median group (4.03 years, 95% CI 4.64-7.99 years) was shorter than that of PWV ratio below median group (10.43 years, 95% CI 9.74-11.12 years, p<0.001). The cardiovascular mortality rate in PWV ratio above median group were significantly higher than that of PWV below median group (log rank test, p<0.001). PWV ratio was a strong and significantly predictor of cardiovascular mortality (HR 2.08 95% CI 1.16-3.71, p=0.014) after adjusting for other confounding factors whereas the CF-PWV was failed to be included as a significant predictor for both all-cause and CVD mortality in the multivariable Cox regression model. This results demonstrated that the discriminative power of the PWV ratio for both all-cause and CVD mortality was better than that of CF-PWV. The present study, to our knowledge, is the first study evaluated the predictive role of PWV ratio in only incident PD patients. We believe that our finding could expand the knowledge in the role of PWV ratio for PD patients' outcomes.

Aortic stiffness is an established predictor for cardiovascular morbidity and mortality. However, in dialysis population, the studies evaluate the predict value of CF-PWV generate conflict results. In a prospective study, Szeto found that a high baseline CF-PWV was associated with a longer overall survival of PD patients but the prognostic value of CF-PWV disappeared after adjusting for clinical confounding factor [9]. The conflict results of that association between arterial stiffness assess by CF-PWV implied that CF-PWV may not be a very good indicators of arterial stiffness for PD patients. The PWV ratio could represent the loss of the normal gradient in arterial compliance. Physiologically, the aorta is much more elastic than peripheral muscular arteries, causing an increase in arterial stiffness (stiffness gradient) from the heart to the periphery. This physiological gradient of arterial stiffness results in a gradual attenuation of the forward pressure wave throughout its passage along the arterial tree down to the microcirculation, where pulsatility is minimal. In normal aging, aortic stiffness increases to a greater extent than that of the peripheral muscular arteries, resulting in equalization or even reversal of the stiffness gradient (aortic stiffness > muscular artery stiffness), which results in higher pulse pressure transmission into the microcirculation, leading to a vascular myogenic response, endothelial dysfunction, hypoperfusion, and organ damage. Unlike CF-PWV, PWV ratio were initially proved to have additional prognostic value in the population of dialysis. Our study further demonstrated its important prognostic role in PD patients. In another our recent study in chronic kidney disease (CKD) population, we found that PWV ratio was significantly related to patient outcome in CKD stage 1–4 patients. However, when we compared the predictive value of PWV ratio with that of the CF-PWV for outcome of CKD, the predictive value of CF-PWV was slightly stronger than that of the PWV ratio. Interestingly, in this study, patients with advanced CKD and higher PWV ratios had a significantly higher risk of adverse CKD outcome. Therefore, we think PWV ratio may be served as a more important and informative indicators for CVD outcomes than CF-PWV along especially in dialysis population or in advanced CKD patients which may due to accelerated aging vessels in these patients.

In summary, we proved PWV ratio, a new arteries stiffness parameter which represent the loss of the normal gradient in arterial compliance is a significant prognostic indicator of CVD mortality in PD patients. Most importantly, we demonstrated that the discriminative power of the PWV ratio for both all-cause and CVD mortality in PD was better than that of CF-PWV.

References
Caregiver burden, defined as stress or strain related to caregiving, can have adverse outcomes for caregivers including psychosocial implications such as higher prevalence of depression, social isolation and suicide [1]. There can also be implications for caregiver’s physical health including sleep deprivation, poor self-care and increased mortality [2]. Caregiver burden can also have implications for the patient’s outcomes [3] as caregivers become burnout and struggle to support the patient in managing their health. Increased caregiver burden is also related to decreasing health-related quality of life (QoL) which is an indicator of how patients and caregivers are coping with the diagnosis and treatment. Poor QoL has been linked to poorer clinical outcomes, including increased mortality [4].

Although peritoneal dialysis (PD) is advocated as a home-based treatment which can be conducted independently by patients, the responsibility of delivering and managing PD is often shared by informal caregivers or family members [5].

The role of caregivers of PD patients can be substantial. Tasks may include preparing the home environment for PD, the self-management aspects of PD (including diet, medication etc.), monitoring adherence, communicating and engaging with health services [6]. In assisted PD, all dialysis-related procedures rely on caregivers. Although formal care resources may be in place – in most settings these may be limited or sporadic. The many types of responsibilities placed on caregivers make caregiving a complex experience that can adversely affect their physical and emotional health. Besides the tasks per se, PD caregivers may also experience significant changes to their lifestyles due to providing care as they may have to prioritise the support of the patient each day, compared with their own needs or wants. This can lead to increased pressure on the caregivers, difficulties in adjusting or accepting of their changed circumstances including loss of income for some, and a decrease in self-care of themselves.

Caregivers of PD patients, compared with haemodialysis (HD) patients show significantly increased caregiver burden. This is particularly in domains around the environment and general strain experienced by caregivers [7]. Caregivers of PD patients also report higher levels of depression and poorer physical symptoms compared with HD caregivers. This is despite a higher satisfaction with the care they are receiving and treatment delivery [8]. Caregiver burden tends also to be increased when caregivers are caring for elderly patients. Caregiver burden is also higher in PD compared with renal transplant patient caregivers [6].

Caregiving in PD is a dynamic process – one can think of it as a journey punctuated by stages. It may begin with the anticipation and preparation for caregiving role (PD training), the performance of tasks, health crises and eventual exit from role. Caregivers may transition into and out of role and the amount and types of care they provide over time may fluctuate. Risks to outcomes may still persist.

A longitudinal study on established PD patients has shown that even though objective caregiving tasks (esp. personal hygiene and PD performance) reduced over 12 months, indicating familiarisation with procedures – overall caregiver burden increased significantly from mild to moderate within the same timeframe. Psychological health too, including emotional QoL significantly decreased [9]. Mental health deterioration was also increased in PD caregivers of highly dependent patients from initiation to 12 months, relative to PD caregivers of less dependent patients [10].

The paradoxical poor emotional outcomes despite the reduced task-involvement suggest that burnout is a real threat for PD caregivers. While PD caregivers may be able to adapt to the performance of tasks, sustaining emotional resilience in longer term is more challenging. Long term caregiver burden is not directly related to tasks, but may be related to the perceived responsibility and worry of supporting a PD patient. This may be due to the caregivers struggling to accept the longevity of the changes to theirs and the patients’ lifestyle. These study findings also highlight the need to regularly monitor and support caregivers beyond the immediate period following PD initiation. The effects on caregivers QoL, may not be apparent immediately, suggesting a ‘honeymoon period’ in perceived burden when assuming the role of a caregiver for a patient on PD.

There is a clear need to explore the ways in which PD caregivers can be better supported alongside patients. Interventions to support caregivers should focus on the emotional aspects of burden, rather than on the task based activities, particularly beyond the initiation of PD treatment. These interventions should also explore how to connect families, with peer support or access to psychological support to help with them managing the acceptance of the longevity of treatment and uncertainty over the future. Due to the challenges PD caregivers may have in attending face to face support, digital or eHealth, based interventions could provide a more accessible platform. Digital interventions could also provide timely access to advice or support for patients as they are delivered within PD caregiver’s homes and can be available to be accessed when required. To support PD patients, digital interventions could focus on improving communication pathways between caregivers.
Learning from Thailand PD First Policy, how we can apply for Nepal

Sanjaya Adhikari
PD Programme Clinical Coordinator, Nepal.

Before the policy was implemented in Thailand there were three health care schemes existed in which Universal Health Coverage Scheme covered majority of population but did not include RRT on it and the others had discrimination to access dialysis as dialysis therapy was expensive, and there was a shortage of supply and medical expertise.

Currently three key strategies (knowledge creation, social mobilization and political involvement) towards PD first were developed. It makes all Thai people access to RRT; the number of patients increased from 600 to 21000 on PD after the policy with more PD centers and trained manpower. Supply is now convenient, price lower through auction process by Government Pharmaceutical Organization. National Health Security Office encourages patients to do their dialysis at home providing free supply to doorstep. It gives good health outcome and reduces the national budget pressure.

I am able to learn about the technique for training medical staff and patients, complication management, data management & its centralization, surgical techniques for TK insertion and its complication management (Bedside TK, outflow management etc).

As the global trend of increasing ESRD population, Nepal is also suffering. Only 20 % of population is able to access RRT. It is because of difficult geography (Mountain & Himalaya), supply problems, lack of manpower, lack of RRT centers, lack of awareness and interest on PD. As I learn from PD policy in Thailand it is best suitable therapy for Nepal because it doesn’t need high technology, need less number of medical personal and cheaper too. As “free dialysis to all deprive citizen” is already announced but developing infrastructure for hemodialysis is expensive. So centrally purchase and distribution of PD fluid, organizing training and awareness about PD will be faster and cheaper method to address maximum ESRD population with RRT. Implementation of National PD program may reduce the budget for free dialysis and can use for ESRD prevention. National PD program can be started from existing government dialysis centers and later to private and community level appointing regional hospitals as training and referral centers.
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ISPD and EuroPD will be jointly hosting the 2020 Congress in Glasgow, Scotland, from 2-5 May. This will be the largest gathering of PD experts in Europe. It is expected to attract over 2,000 delegates from around the world.

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Local Experience: PD Supervisory Visit - A Preliminary Result from Thailand

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Since an adoption of “peritoneal dialysis (PD) first” policy in 2008, the number of PD patients in Thailand has exponentially raised to a level of 50,000 cases in 2019. With this tremendous expansion, Thailand, a middle income country, has faced many challenges including but not limited to insufficient infrastructure, financial burden, misperception of PD quality, and nursing shortage. To ensure that our patients have received high-quality PD treatment comparable with internationally acceptable standard, six organizations, including Nephrology Society of Thailand (NST) together with Thai Nephrology Nursing Association, Thai Dietetic Association, Thai Pediatric Nephrology Association, Ministry of Public Health (MOPH), and National Health Society Organization have joined and taken initiative to conduct “2-day PD supervisory visit” in all 13 healthcare regions in Thailand year 2018-2019. This visit begins the first day with representative of an individual PD center from the same region presenting their PD programs, mission, center’s needs and obstacles, and -- most importantly -- self-assessment on 8 PD key performance indicators (KPI). On second day, selected PD centers were visited by the evaluator team to assess a strengthening of multidisciplinary care team. This is a forum for PD nurses, physicians, pharmacists, dieticians, and medical directors to share data, transfer experiences, exchange knowledge and problems, and find solutions together. Thus far, we have had the supervisory visits covering eleven health care regions in Thailand. We have received positive feedbacks from health care professionals and other stakeholders.

Based on preliminary data, the major obstacle faced by most programs is a high burden of PD healthcare workers. Only 55% and 51% of PD centers participated in the supervisory visit program achieved the target of PD nurse to patient ratio below 1:50 and the target of physician to patient ratio below 1:100, respectively. This issue should be urgently addressed to ensure the sustainability of the PD centers in Thailand.

Impact of Body Fat Accumulation on Prognosis in PD Patients

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Patients with end-stage renal disease (ESRD) generally experience significant weight gain after initiating peritoneal dialysis (PD), and a large proportion of PD patients become obese during the course of PD treatment. Significant weight gain and detrimental fat accumulation often occurs shortly after initiating PD, within 1 - 2 years [1, 2]. This may be an inevitable consequence of increased caloric intake secondary to continuous dialysate glucose absorption through the peritoneum [3, 4]. Unfortunately, this can result in potentially serious problems such as obesity-related cardiometabolic complications or severe emotional distress caused by the visible changes in body shape and appearance. To date, no consensus has been reached as to whether new-onset obesity, regardless of baseline BMI, has an impact on the long-term survival of PD patients. Previous studies have shown that there is a positive association between increased BMI and survival in those undergoing hemodialysis (HD) [5]; however, the reverse epidemiology of HD patients should not be extrapolated easily to those receiving PD because the BMI increase in PD patients are mainly caused by higher fat mass, visceral obesity, and/or fluid overload [6]. All of these factors can contribute to increased production of pro-inflammatory cytokines, a rapid loss of residual renal function, and an altered lipid profile [7-9].

Recently, we evaluated this unsolved issue with a well-controlled PD cohort [10]. Using a longitudinal, repeated measures design, we used bioimpedance analysis to track changes in body fat percentage (BFP). And the long-term effect of excessive fat accumulation (defined as a 1-year change in BFP (ΔBFP) over the highest quartile) on patient survival and PD failure rates was analyzed. As we focused primarily on establishment of the prognostic value of fat mass changes, all survival analyses reported in this study applied to the follow-up period after the second bioimpedance test, regardless of PD start date. According to our data, patients experienced an overall weight gain of 2 kg (3.0%) and fat gain of 1.8% per year (IQR, -3.2, 5.4) during the early period of PD treatment. This degree of weight gain seems to be much lower than that of Western countries, which is reported to be as high as 6 - 10% [11,12]. This might be influenced by differences in diet, exercise, or race. Interestingly, patients with excessive fat gain (5.0% for men, 5.4% for women) had a higher mortality rate than those with modest fat gain.
evertheless, the excessive acquisition of body fat was strongly associated with worse outcomes, independently of baseline obesity and fluid status, and it represents an emerging risk factor for long-term prognosis. Therefore, we believe that close, repeated monitoring of fat mass or fat percentage could provide additional significant prognostic information beyond what a single measurement can provide, especially in incident PD patients to minimize obesity-related metabolic complications. Supporting this, obese ESRD patients who are metabolically healthy are known to have a lower risk of mortality than their normal-weight counterparts. However, no mortality benefit exists in obese and metabolically unhealthy ESRD patients [12].

In addition, excessive fat accumulation also increases the rate of PD failure. Interestingly, baseline obesity and excessive fat gain independently affected the rate of transfer to HD. In other words, obese patients with excessive fat accumulation during the early period of PD showed the highest risk of transfer to HD. Possible explanations for these findings are that abdominal obesity-related changes in peritoneal characteristics may affect the PD failure rate, or that fat accumulation in the peritoneal membrane may induce peritoneal inflammation, fibrosis, peritoneal fatty infiltration, and peritoneal thickening. When measuring peritoneal characteristics, but we did not observe any changes associated with excessive fat accumulation. We believe this was likely to be due to the relatively short follow-up period of this study. However, in patients who had received PD for > 2 years, changes in body weight or BFP were not statistically significant, and the effects of baseline comorbid conditions on body composition changes were attenuated. Also, changes in body weight and body fat were not significantly associated with patient prognoses, even in those patients with excessive fat gain. This could be a survival-related bias or could represent the importance of malnutrition and inflammation rather than fat gain in the chronic PD group.

In conclusion, becoming obese shortly after initiating PD does not merely involve a change in body shape, it could be an indicator of poor prognosis. To maintain metabolic health in PD patients, care should be taken to minimize early increases in fat mass by reducing peritoneal glucose absorption, providing education on a proper diet, and emphasizing regular exercise.

References

Editor’s Note

The ISPD Asia-Pacific Chapter meeting is coming. Go and get registered. See you in Nagoya!

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Sincerely,

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