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Frailty among hemodialysis patients

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A B S T R A C T

Introduction: Hemodialysis patients have physical vulnerability due to the progressive decline of the body's systems. The physical changes in the patients can lead to haemostatics failure, known as frailty syndrome. The frail condition can cause maladaptive psychological responses due to changes that can cause anxiety in patients.

Objective: This study aims to determine the prevalence of frailty in hemodialysis patients and the different factors that correlate with frailty patients undergoing hemodialysis therapy.

Method: This is a cross-sectional study involving 55 respondents who underwent hemodialysis therapy at the Jember Klinik Hospital. The instruments used in this study were the Edmonton Frail Scale (EFS) and the Hamilton Anxiety Rating Scale.

Results: Moderate frailty was found in 23 patients (41.8%), followed by mild frailty in 18 patients (32.7%) and severe frailty in 14 patients (25.5%). Patient with frailty was associated with income, educational level, anxiety, and time on hemodialysis in a patient**.**

Conclusion: Frailty was highly prevalent in hemodialysis patients and had relations with anxiety and different sociodemographic characteristics of patients.

INTRODUCTION

Hemodialysis is a therapy for patients with kidney problems. Patients receiving hemodialysis therapy are 92% due to chronic renal failure. Based on the global situation from 79 countries, the average number of new chronic renal failure diagnoses worldwide was 144 individuals per million.[1] In Indonesia, patients with chronic kidney failure, continue to increase annually, where the incidence of chronic kidney failure in 2018 was 0.38% compared to 0.2% in 2013.[2] Furthermore, the number of new patients undergoing hemodialysis therapy in 2018 was 66,443 this is a two-fold increase compared to 30,831 cases in 2017.[3] Patient on hemodialysis continue to bear a high burden of disease, shortened life expectancy, outcome suboptimal, high rates of comorbidities and poor health-related quality of life.[4,5]

Impact of hemodialysis in patients widely known such as decreased kidney function, decreased muscle mass, comorbid conditions, and decreased physical and cognitive function.[6] These clinical conditions can lead to high vulnerability for sudden adverse health or a decrease in the physiological functions from various stressors or the aging process; this concept is called frailty.[7,8] Frailty is a syndrome of the decreased physiological capacity of the body due to the aging process. It impacts reducing resistance to stress and vulnerability to experiencing poor health outcomes.[9] Although the concept of frailty was initially closely related to the elderly; several clinical conditions can deteriorate the frailty in people with chronic kidney disease.[8,10]

In patients with kidney failure who underwent hemodialysis, 14-73% of them had the frailty syndrome.[11] In addition, in frail patients, 1.43 fold higher number of hospitalization independent of age, sex, comorbidity, and disability.[12] The relationship between kidney failure and the incidence of frailty is not fully understood. However, clinical conditions such as chronic kidney failure may limit the patient's fluid

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and nutrient intake due to food restriction and reduce muscle mass due to Physical inactivity, making them at risk of frailty. In addition, an increase in pro-inflammatory cytokines was observed in patients with kidney failure and patients with frailty.[11,13] Frailty in hemodialysis patients has addictive adverse on the clinical outcome.[14] Identifying frailty can provide important prognostic information for providers and patients before and after initiation of dialysis.[5]

In addition to frailty syndrome, alteration of a patient with hemodialysis therapy shows psychological disorders such as anxiety and depression. The prevalence of anxiety disorder among chronic kidney disease patients was around 19,7% to 61% in various studies.[15–17] Anxiety in patients with chronic kidney failure undergoing hemodialysis therapy may be triggered by various stressors, including the experience of pain, financial problems, difficulty in fulfilling job, loss of libido, depression, and fear of death.[18] Anxiety and frailty syndrome are inter-linked. In hemodialysis patients, the phycological disorder makes it challenging to take up a physical activity that can make patients frailer.[19] For this reason, we included the anxiety variable in this study to determine might anxiety can correlate with frailty syndrome.

This study aimed to determine the prevalence of frailty syndrome in kidney failure patients undergoing hemodialysis therapy. We will also analyze the association between frailty syndrome and anxiety in patients undergoing hemodialysis therapy with kidney failure.

METHOD

Study Design

This is a cross-sectional study design.

Setting and Respondent

The population in this study was hemodialysis patients at the Jember Clinical Hospital. 55 Respondent were recruited between January-Maret 2021. The inclusion criteria were patients over 18 years, level of consciousness compos mentis when hemodialysis, and not diagnosed COVID-19. The exclusion criteria in this study were refused as respondent, decreased consciousness, or physiological condition during data collection. All participants provided written informed consent.

The Variable, Instrumen, and Measurement

In the study, Sociodemographic (age, gender, income level, religion, time on hemodialysis, and education) collected used questionnaires through medical reports and participant self-report. In variable Frailty, Status was assessed using the Edmonton Frail Scale (EFS) questionnaire. EFS consists of nine domains (cognition, general health status, functional independence, social support, medication use, nutrition, mood, continence, functional performance). EFS showed inter-rater reliability (k=0.77, p=0.0001, n=18). The internal consistency of the EFS using Cronbach's a was 0.62.[20] Frailty status in EFS is divided into five categories non-frail (0-5), vulnerable (8-9), mild (8-9), moderate (10-11), severe frail (12-17).[21] The variable anxiety was assessed using the HARS (Hamilton Anxiety Rating Scale) questionnaire. HARS questionnaire consists of 14 items, each defined by a series of symptoms, and measures both psychic anxiety (mental agitation and psychological distress) and somatic anxiety (physical complaints related to anxiety). HARS had Crohnbach's (0.921) and Bartlett's test of sphericity = $p < 0.001$.[22] Anxiety classification in HARS divided into five categories not anxiety (0-14), Mild (15-20), Moderate (28-41), Severe (42-56).[23]

Data analysis

Statistical analysis in this study was performed using the Spearman, Lamda, Somers, and Kruskal Wallis test. The data is not normally distributed.

Ethical Consideration

This study had passed the ethics test by the committee of the University of Muhammadiyah Jember with the registration number. 01220/KEPK/FIKES/I/2021.

RESULTS

The study results found that most of the participants had moderate frailty. In this study, a younger age (<60 years) showed more frailness than older age. The male gender showed lower frailty status than females. Income participant level above minimum wage similar in mildly and moderate frail status. Ninety-six percent of the participant was Muslim, and there is no significant correlation between religion and frailty status. The frail condition will increase with age, and the physical condition worsens, but patients who underwent hemodialysis for less than six months also showed a frail condition in this study. Regarding participant education level, 58.2% were senior high school, and 30.9% held a university degree. Table 1 demonstrated that 36.4% of the participant were experiencing severe anxiety, and only 12.7% were not anxious.

Based on table 1, statistical analysis showed that age, gender, religion, and anxiety levels are not significantly correlated with the frailty status of patients undergoing hemodialysis therapy; however, income level (p=0.045), length of time undergoing hemodialysis (p=0.027), an education level (p=0.049) and anxiety (p=0.001) had a significant correlation with frailty status in a hemodialysis patient.

Table 2. Sociodemographic and Clinical Characteristic of Patients by Frailty Status (n=55)

Variable	Frailty Status			Total	p-value
	Mildly Frail (n=18)	Moderate Frail (n=23)	Severe Frail (n=14)		
Age					
<60 years	14 (25.5%)	20 (36.4%)	11 (20.0%)	45 (81.8%)	0.378
>60 years	4 (7.3%)	3 (5.5%)	3 (5.5%)	10 (18.2%)	
Gender					
Male	15 (23.7%)	13 (23.6%)	9 (16.4%)	37 (63.7%)	0.218
Female	3 (5.5%)	10 (18.2%)	4 (9.1%)	18 (32.7%)	
Income level					
Above minimum wage	15 (27.3%)	15 (27.3%)	7 (12.7%)	37 (63.7%)	0.045
Below minimum wage	3 (5.5%)	8 (14.5%)	7 (12.7%)	18 (32.7%)	
Religion					
Muslim	18 (32.7%)	21 (38.2%)	14 (25.5%)	53 (96.4%)	0.850
Catholic	0 (0%)	1 (0%)	0 (0%)	1 (1.8%)	
Protestant	0 (0%)	1 (0%)	0 (0%)	1 (1.8%)	
Time on Hemodialysis					
>6 months	4 (7.3%)	0 (0%)	0 (0%)	4 (7.3%)	0.027
<6 months	14 (25.5%)	23 (41.8%)	14 (25.5%)	51 (92.7%)	
Education level					
Not going to school	0 (0%)	1 (1.8%)	1 (1.8%)	2 (3.6%)	
Primary school	0 (0%)	2 (3.2%)	1 (1.8%)	3 (5.5%)	0.049
Junior high school	0 (0%)	0 (0%)	1 (1.8%)	1 (1.8%)	
Senior high school	11 (20.0%)	12 (21.8%)	9 (16.4%)	32 (58.2%)	
University	7 (12.7%)	8 (14.5%)	2 (3.2%)	17 (30.9%)	
Anxiety					
Not anxious	2 (3.6%)	3 (5.5%)	2 (3.6%)	7 (12.7%)	
Mild	3 (5.5%)	5 (9.1%)	4 (7.3%)	12 (21.8%)	0.001
Moderate	7 (12.7%)	7 (12.7%)	2 (3.6%)	16 (29.1%)	
Severe	6 (10.9%)	8 (14.5%)	6 (10.9%)	20 (36.4%)	

DISCUSSION

Frailty is defined as a failure to repair homeostasis after experiencing specific stress.[9] Stress on hemodialysis patients is caused by a clinical change that can make the patient more vulnerable. Based on this study, the frailty status of patients undergoing hemodialysis therapy showed that most participants have moderate frail (41.8%) and mild frail (32.7%). In their systematic review, Chowdhury et al. report that frailty was more prevalent amongst patients on hemodialysis, ranging from 14-73%.[11] This result is appropriate with our finding that more than sixty percent of patients have moderate or severe frailty. Clinical conditions cause frailty in hemodialysis patients to change, such as limitation of fluid and nutrients and physical inactivity that makes them at risk of frailty.[13] In addition, other conditions that can worsen frailty status were anemia, sarcopenia, fall/fracture, vascular disease, cognitive impairment, functional impairment, and decreased physiological reserve.[24] Based on EFS results in our research, most participants got high scores in domain-general health status, functional independence, medication use, mood, and functional performance. This domain can indicate that frail patients have a problem with their health status because most patients have been hospitalized more than twice in one year. Besides, medication received by the patient has more than five types, and patient compliance in treatment needs to be studied further. This condition can worsen and affect the patient's outcome because frailty was associated with poor short-term outcomes and higher mortality rates, gustatory dysfunction, quality of life, fatigue visits to hospital emergency services, hospitalization.[21,25,26]

Anxiety was a common yet frequently overlooked psychological disorder in patients treated with hemodialysis.[15,27] In our study, most patients with hemodialysis report that eighty percent of patients had anxiety from mild to moderate. This result following Gadia et al. showed anxiety disorder in chronic kidney disease happens in 61% of patients. In hemodialysis patients, anxiety happens because of changes that occur due to decreased kidney function. Several causes of anxiety in patients with kidney failure who underwent hemodialysis therapy are physical changes due to clinical manifestations of hemodialysis such as physical weakness, palpitations, tremors, indigestion, shortness of breath, nervousness, edema, and diaphoresis. Psychosocial changes such as feeling helpless, depressed, and restless are other causes of anxiety in hemodialysis therapy patients.[18] Based on our analysis from HARS questioner symptoms of anxiety in hemodialysis patients in a dimension cardiovascular, genitourinary, and autonomic symptoms happed caused by a physiological change in a patient not impact from an anxiety disorder. In addition to clinical change or the impact of anxiety, anxiety in hemodialysis patients is associated with poorer quality of life.[17,28]

Patients undergoing hemodialysis therapy with various physical, social, and spiritual problems will reduce the patient's quality of life.[27] Based on the results of the statistical tests, we found variables that have a significant association and some variables that do not have a significant association with frailty. We categorized the patient's age into more than 60 years and less than 60 years to distinguish the effect of frailty on the elderly and non-elderly groups ($p>0.05$). The results of this study are in line with the results of a study by Canton et al., which showed that age did not affect patients with heart failure who had frailty or did not have frailty.[21] The association between age and frailty status is related to a decrease in body function in the elderly due to aging processes. In this study, the frailty status was assessed using the Edmonton Frailty Scale, and the test showed that patients who aged more than 60 years had mild, moderate, and severe frailty. The results also showed almost the same proportion, ranging from 5.5% to 7.3%. This means that the elderly did not experience a worsening frailty status.

Gender also did not show significant ($p>0.05$). Women have a higher prevalence of frailty than men. This is because women have a lower mean of muscle mass and strength.[7] The study by Canton et al. showed a non-significant association of gender variables in patients who experienced frailty ($p>0.05$).[21] In this study, most patients were male (67.3%), meaning that the female patients were poorly represented. We analyzed that males had higher peak bone mineral density and muscle mass, and also, in males, they have a slower rate of losing muscle and bone to maintain their strength.[29]

In the time on hemodialysis variable, the statistical results showed a p-value of 0.027 ($p<0.05$) (Table 1), meaning that the variable had a significant relationship with frailty status. Long-term time hemodialysis patients can decrease their body. This is also associated with the patient's ability to perform health management. The results of this study are also in line with the research of Mc Adam et al., which showed a relationship between the length of undergoing dialysis in months with frailty.[12] In patients with kidney failure undergoing hemodialysis therapy, frailty status can predict the outcomes. About 40% of patients with frailty showed a high mortality rate at the third year of undergoing hemodialysis.[13]

This study found a significant relationship between educational level with frailty status. This level of education is also correlated with the level of income of participants where they have income above the minimum limit to study well. Both of these variables have a correlation with frailty status in hemodialysis patients. Several studies have shown that education and income affect a person's frail status, although there is no definite reason for correlating these two variables.[31,32] The complexity of frail status in functional independence requires high cognitive skill, which can be negatively influenced by poor frail status. Other possible reasons include that educational level can lead to barriers in communication, which creates difficulties for engagement in more complex activity.[30]

Anxiety and frailty status in patients with kidney failure will predict clinical outcomes in patients undergoing hemodialysis and affect their quality of life.[5] We found limited data related to anxiety and frailty status in patients with kidney failure. This study observed a difference between frailty and anxiety between patients with mild and severe frailty. Anxiety in this study is most often accompanied by severe anxiety (36.4%), but the most frequent category of frailty variables is moderate frailty (41.8%). This difference shows that patients who have a higher risk of frailty also increase anxiety scores (Tabel 2). Pathophysiologically, frailty and anxiety are predictors of the clinical outcomes in patients with kidney failure, especially regarding the patient's quality of life. The incidence of frailty and anxiety in patients with kidney failure can be caused by various factors, including changes in physical functions. Despite frailty's strong associations with poor outcomes for patients with ESRD, frailty is not routinely assessed clinically.[32] Therefore, in patients with kidney failure, specific screening for physical and psychological symptoms should be taken into account and can be used to predict survival and better inform the shared decision-making process for patients with advanced kidney disease.[26,33–36]

This study had several limitations. First, a relatively small group was studied, and the patient was the same as of hemodialysis service, so a variety of patients were needed from the other hemodialysis center. Second, this study was not randomized. Third, a control group was needed, especially on the difference between elderly and non-elderly respondents because the concept of frailty is more widely used in the elderly.

CONCLUSIONS AND RECOMMENDATION

This study revealed that frailty is hight prevalent in hemodialysis patients. Our study also found that frailty was associated with income, educational level, anxiety, and time on hemodialysis. Frailty screening for patients undergoing hemodialysis is essential. Future studies should specifically explore the impact of frailty on hemodialysis patients and nursing interventions that can prevent it.

REFERENCES

1. Kemenkes RI. *Hasil Riskesdas 2018*.; 2018. Accessed December 29, 2021. http://labdata.litbang.kemkes.go.id/images/download/laporan/RKD/2018/Laporan_Nasional_RKD2018_FINAL.pdf
2. Thurlow JS, Joshi M, Yan G, et al. Global epidemiology of end-stage kidney disease and

disparities in kidney replacement therapy. *American Journal of Nephrology*. 2021;52(2):98-107. doi:10.1159/000514550
3. PERNEFRI. *11th Report Of Indonesian Renal Registry 2018*.; 2018. https://www.indonesianrenalregistry.org/data/IRR2018.pdf
4. Himmelfarb J, Vanholder R, Mehrotra R, Tonelli M. The current and future landscape of dialysis. *Nature Reviews Nephrology*. 2020;16(10):573-585. doi:10.1038/s41581-020-0315-4
5. Sy J, Johansen KL. The impact of frailty on outcomes in dialysis. *Curr Opin Nephrol Hypertens*. 2019;176(3):139-148. doi:10.1097/MNH.0000000000000364.
6. Johansen KL, Chertow GM, Jin C, Kutner NG. Significance of frailty among dialysis patients. *Journal of the American Society of Nephrology*. 2007;18(11):2960-2967. doi:10.1681/ASN.2007020221
7. Wistara ANA. Studi komparasi kejadian frailty pada populasi lansia di Desa Pedawa Singaraja dan Kota Mangupura Badung Provinsi Bali. *Medicina*. 2019;50(1):41-45. doi:10.15562/medicina.v50i1.325
8. Van Munster BC, Drost D, Kalf A, Vogtlander NP. Discriminative value of frailty screening instruments in end-stage renal disease. *Clinical Kidney Journal*. 2016;9(4):606-610. doi:10.1093/ckj/sfw061
9. Laksmi PW, Liwang F, Marcelina R. Management of Frailty As a New Geriatric Giant : How To Deal With Dilemmatic Health Problems in Elderly Patient. In: *Prosiding Temu Ilrniah Geriatri 2015. Perhimpunan Gerontologi Medik Indonesia Cabang Jakarta*. ; 2015
10. Hiriscau EI, Bodolea C. The Role of Depression and Anxiety in Frail Patients with Heart Failure. *Diseases*. 2019;7(2):45. doi:10.3390/diseases7020045
11. Chowdhury R, Peel NM, Krosch M, Hubbard RE. Frailty and chronic kidney disease: A systematic review. *Archives of Gerontology and Geriatrics*. 2017;68:135-142. doi:10.1016/j.archger.2016.10.007
12. McAdams-Demarco MA, Law A, Salter ML, et al. Frailty as a novel predictor of mortality and hospitalization in individuals of all ages undergoing hemodialysis. *Journal of the American Geriatrics Society*. 2013;61(6):896-901. doi:10.1111/jgs.12266
13. Nixon AC, Bampouras TM, Pendleton N, Woywodt A, Mitra S, Dhaygude A. Frailty and chronic kidney disease: Current evidence and continuing uncertainties. *Clinical Kidney Journal*. 2018;11(2):236-245. doi:10.1093/ckj/sfx134
14. Szeto CC, Chan GCK, Ng JKC, et al. Depression and Physical Frailty Have Additive Effect on the Nutritional Status and Clinical Outcome of Chinese Peritoneal Dialysis. *Kidney and Blood Pressure Research*. 2018;43(3):914-923. doi:10.1159/000490470
15. Mosleh H, Alenezi M, al johani S, Alsani A, Fairaq G, Bedaiwi R. Prevalence and Factors of Anxiety and Depression in Chronic Kidney Disease Patients Undergoing Hemodialysis: A Cross-sectional Single-Center Study in Saudi Arabia. *Cureus*. Published online January 15, 2020. doi:10.7759/cureus.6668
16. Rahman S, Pradido R. The anxiety symptoms among chronic kidney disease patients who undergo hemodialysis therapy. *International Journal of Public Health Science (IJPHS)*. 2020;9(4):281-285. doi:10.11591/ijphs.v9i4
17. Gadia P, Awasthi A, Jain S, Koolwal G. Depression and anxiety in patients of chronic kidney disease undergoing haemodialysis: A study from western Rajasthan. *Journal of Family Medicine and Primary Care*. 2020;9(8):4282. doi:10.4103/jfmpc.jfmpc_840_20
18. Dwi M, Santoso Y. Tinjauan Sistematik: Kecemasan Pada Pasien Gagal Ginjal Kronik dengan Tindakan Hemodialisis. *JK Mesencephalon*. 2018;4(2):99-105.
19. Hornik B, Duława J. Frailty, quality of life, anxiety, and other factors affecting adherence to physical activity recommendations by hemodialysis patients. International Journal of Environmental Research and Public Health. 2019;16(10). doi:10.3390/ijerph1
20. Petty DR, House A, Knapp P, Raynor T, Zermansky A. Validity and reliability of the Edmonton Frail Scale. *Age and Ageing*. 2006;35(5):523-526. doi:10.1093/ageing/afl023
21. Garcia-Canton C, Rodenas A, Lopez-Aperador C, et al. Frailty in hemodialysis and prediction of poor short-term outcome: mortality, hospitalization and visits to hospital emergency services. Renal Failure. 2019;41(1):567-575. doi:10.1080/0886022X.2019.1628
22. Hallit S, Haddad C, Hallit R, et al. Validation of the Hamilton Anxiety Rating Scale and State Trait Anxiety Inventory A and B in Arabic among the Lebanese population. Clinical Epidemiology and Global Health. 2020;8(March):1104-1109. doi:10.1016/j.cegh.20
23. Clark DB, Donovan JE. Reliability and validity of the Hamilton Anxiety Rating Scale in an adolescent sample. *Journal of the American Academy of Child and Adolescent Psychiatry*. 1994;33(3):354-360. doi:10.1097/00004583-199403000-00009
24. Portilla Franco ME, Molina FT, Gregorio PG. Frailty in elderly people with chronic kidney disease. *Nefrología (English Edition)*. 2016;36(6):609-615. doi:10.1016/j.nefroe.2016.12.005
25. Nixon AC, Bampouras TM, Pendleton N, Mitra S, Brady ME, Dhaygude AP. Frailty is independently associated with worse health-related quality of life in chronic kidney disease: A secondary analysis of the Frailty Assessment in Chronic Kidney Disease study. *Clinical Kidney Journal*. 2019;13(1):85-94. doi:10.1093/ckj/sfz038
26. Chen SI, Chiang CL, Chao C Ter, Chiang CK, Huang JW. Gustatory Dysfunction Is Closely Associated With Frailty in Patients With Chronic Kidney Disease. *Journal of Renal Nutrition*. 2021;31(1):49-56. doi:10.1053/j.jrn.2020.06.006
27. Cohen SD, Cukor D, Kimmel PL. Anxiety in patients treated with hemodialysis. *Clinical Journal of the*

American Society of Nephrology. 2016;11(12):2250-2255. doi:10.2215/CJN.02590316

28. Peltzer K, Pengpid S. Anxiety and depressive features in chronic disease patients in Cambodia, Myanmar and Vietnam. *South African Journal of Psychiatry*. 2016;22(1):1-4. doi:10.4102/sajpsychiatry.v22i1.940
29. Morley JE, Kim MJ, Haren MT, Kevorkian R, Banks WA. Frailty and the aging male. *Aging Male*. 2005;8(3-4):135-140. doi:10.1080/13685530500277232
30. Brigola AG, Alexandre TDS, Inouye K, Yassuda MS, Pavarini SCI, Mioshi E. Limited formal education is strongly associated with lower cognitive status, functional disability and frailty status in older adults. Dementia e Neuropsychologia. 2019;13(2):216-224
31. Apriliani A. Hubungan Karakteristik Demografi Dengan Frailty Di Kota Malang. Published online 2017.
32. Salter ML, Gupta N, Massie AB, et al. Perceived frailty and measured frailty among adults undergoing hemodialysis: A cross-sectional analysis. *BMC Geriatrics*. 2015;15(1):1-7. doi:10.1186/s12877-015-0051-y
33. Hornik B, Duława J. Frailty, quality of life, anxiety, and other factors affecting adherence to physical activity recommendations by hemodialysis patients. International Journal of Environmental Research and Public Health. 2019;16(10). doi:10.3390/ijerph1
34. Worthen G, Tennankore K. Frailty screening in chronic kidney disease: Current perspectives. *International Journal of Nephrology and Renovascular Disease*. 2019;12:229-239. doi:10.2147/IJNRD.S228956
35. Pugh J, Aggett J, Goodland A, et al. Frailty and comorbidity are independent predictors of outcome in patients referred for pre-dialysis education. *Clinical Kidney Journal*. 2016;9(2):324-329. doi:10.1093/ckj/sfv150
36. Morton S, Isted A, Avery P, Wang J. Is Frailty a Predictor of Outcomes in Elderly Inpatients with Acute Kidney Injury? A Prospective Cohort Study. *American Journal of Medicine*. 2018;131(10):1251-1256.e2. doi:10.1016/j.amjmed.2018.03.012