

Lowering dialysis sessions duration may be dangerous

(Les dangers potentiels de la diminution de la durée des séances de dialyse)

Jacques Chanliau¹ Pierre-Yves Durand²

¹Pôle Domicile - AURAL – 124 Rue Villon. LYON 69008 ²Service de néphrologie - Hôpital Edouard Herriot – Hôpitaux Civils de Lyon – 5 place d'Arsonval, LYON 69003

Note : ce texte est disponible en Français à la même adresse url : https://doi.org/10.25796/bdd.v4i1.60263

Résumé

La diminution de la durée des séances de dialyse, peut-être par souci d'amélioration de la qualité de vie du patient, ou peut-être pour optimiser la gestion des établissements de dialyse peut éventuellement avoir des répercussions négatives sur la qualité du traitement et de la qualité de vie du patient.

Un certain nombre d'arguments, listés dans ce travail, sont en faveur de cette hypothèse, et nous arrivons à la conclusion de la nécessité de limiter l'intervalle de temps entre les dialyses par des dialyse plus longues ou plus fréquentes que ce qui est fait actuellement.

Les difficultés d'organisation des établissements pour répondre à ce besoin montrent la nécessité de développer à nouveau la dialyse à domicile.

Summary

Dialysis session in less duration - either to give a better quality of life for the patient or to optimize the organization the dialysis institution - may have bad repercussions on the quality of the treatment and therefore the quality of life of the patient.

According to the result of the publications listed in this work, we conclude that it is necessary to perform either longer sessions or more frequent treatments to limit the interval time between two sessions.

As this is difficult to perform by the providers, we recommend to develop home dialysis to obtain the best result.

Mots clés : hémodialyse, durée dialyse, prescription dialyse

Key words : hémodialysis, dialysis duration, dialysis prescription

In the 1980s, the average length of a hemodialysis session was five hours. "Long" dialysis was defined as dialysis lasting more than six hours, and four-hour sessions were characterized as short. In 2021, the qualification of an ideal duration of a dialysis session remains unclear. This review analyzes the evolution of practices through the prism of technological developments and scientific knowledge, allowing for the emergence of a notion that may be more appropriate on the physiological level: the interdialytic time interval.

In 2021, what is the "standard" length of hemodialysis sessions?

More than 60 years after the invention of hemodialysis, the duration and/or frequency of sessions remains questionable. The first American study by the National Cooperative Dialysis Study Group (NCDS), published in 1981, failed to establish a link between patient morbidity and duration of sessions [1]. The second major NCDS study, published in 1985, established the Kt/V of urea as the main marker of adequacy [2]. Based on these data, the goal was to deliver highly efficient dialysis to achieve the target Kt/V with the shortest sessions possible. In the following decade, focused on this single indicator, prescribers drastically reduced the average duration of hemodialysis sessions, from 6–8 hours to 2.5–4 hours [3]. However, in 2002, the Hemodialysis Study Group (HEMO) did not confirm improvements in patient survival after an increase in Kt/V, with constant dialysis duration [4]. Consequently, the debate on the duration of the sessions reemerged, with studies producing contrasting results. Some studies showed an improvement in survival with long dialysis [5–7], but these results were not confirmed by other studies [8].

In the absence of a medical consensus on the minimum duration and frequency of hemodialysis sessions, managers participated in the discussions. The economic interest of short dialysis was opposed to medical will, with effectiveness more or less depending on the influence of learned societies in different countries. For example, long dialysis is subject to penalties in the UK, incentives in Japan, and regulations in Germany [41].

In France, with the decrees of 2002, legislators wished to avoid abuses of short dialysis by limiting the number of sessions per day and per shift [9]. In 2012, quality criteria for dialysis were established by the Haute Autorité de Santé. Among these, Indicators for the Improvement of Quality and Safety of Care (IPAQSS in French) criteria integrated the duration and frequency of hemodialysis sessions. The minimum goal was set at 3 sessions and 12 hours per week of dialysis. The IPAQSS campaigns from 2012 to 2018 opposed the temptation of establishments and prescribers to reduce the number and duration of sessions. However, despite these incentives, the observed trend was to reduce the frequency and duration of dialysis sessions (Table 1). In 2020, the average duration of sessions is 3 hours 54 minutes with a decreasing trend. The proportion of sessions lasting longer than 4 hours is decreasing, and that of sessions lasting less than 3 hours is increasing. More patients are doing less than 3 sessions per week. However, the mortality of dialysis patients in France did not worsen between 2012 and 2018 (Table 1).

and 2018 data [10, 11]		
	2012	2018
GFR median at dialysis initiation	8.9	9.2
BMI median at dialysis initiation	25.5	25.9
Average duration of dialysis sessions	237 ± 30 mn	234 ± 30 mn
< 2 session / week	3.6%	3.7%
3 session / week	94%	93%
Sessions > 4 hours	11%	8%
Sessions < 3 hours	1%	1.7%
Mortality rate (for 100 patients-years)	16.7	15.9

◆ Table 1. Evolution of patient characteristics and dialysis prescriptions between 2012 and 2018. REIN Registry, 2012 and 2018 data [10, 11]

GFR = glomerular filtration rate (mL/mn/1.73m2); BMI = body mass index (Kg/m2)

The IPAQSS were abandoned for dialysis in 2019. The decrees of 2002 are in the process of revision, with an overhaul of the dialysis authorization regime, which could lead to a deregulation of supply. There will therefore no longer be any incentive to prescribe a minimum thrice-weekly dialysis and/or four hours or more. In 2020, the average duration of hemodialysis sessions was less than four hours (Table 1).

The temptation of short dialysis

- Patients want to reduce the length of their sessions

The strain of dialysis is a heavy burden that patients often want to alleviate by spending less time. Nephrologists are pressured daily by their patients to shorten dialysis sessions. Over the past two decades, cultural, social, and legal developments have profoundly changed doctor-patient relationships. Legislators have upheld patients' rights, particularly the right to refuse treatment. The law of March 4, 2002, on patients' rights allows patients to choose their treatment and possibly express an opposable refusal. From now on, the role of the nephrologist would be to inform and propose, and that of the patient is to choose the duration of their session. Often, the patient's experience corresponds with a session whose duration is increased because of significant hyperhydration, causing, especially at the end of dialysis, episodes of drops in blood pressure, vomiting, and cramps when the rate of hourly ultrafiltration was not suited to increasing the duration of the session. Thus, patients conclude that they cannot stand dialysis for more than four hours. However, if dialysis is not supported, it is paradoxical that it is too short to obtain the dry weight, which requires a reduction in the hourly ulrafiltration (UF)rate under these conditions. The few patients convinced of the benefits of long or daily dialysis are those who have experienced these modalities themselves.

- Facility managers are encouraged to reduce the duration of sessions

Shortening the duration of sessions allows managers of dialysis centers to optimize the financial management of staff and premises. The resulting savings are thus substantial. The managers argue for the reduction in reimbursement rates for dialysis, which was nearly 15% between 2014 and 2019 for in-center dialysis [12]. However, the profitability of dialysis is declining more slowly than the prices. The reports of the court of auditors denounced "the scandalous profitability of dialysis treatments in its various forms, but especially for dialysis in outpatient centers"

[13]. Virtuous managers retain organizational flexibility, allowing long dialysis or using the profit margins of the center to finance deficit techniques such as daily home hemodialysis or long-night dialysis. As a result, virtuous managers are the most affected by reductions in reimbursement rates. Other managers have already set up rigid schemes that no longer allow the prescription of sessions more than four hours.

- Nephrologists are encouraged to reduce the duration of sessions

The decrees of 2002 defined a significant workload for nephrologists particularly by requiring them to be permanently present at the center for the duration of the sessions [9]. In a context of structurally insufficient demographics, dialysis nephrologists are sometimes reluctant to increase the length of sessions, which means overtime on already busy days. The work overload associated with medical presence is the same for a single patient with long dialysis as for several. As a result, the standardization of a maximum session duration for all has become the norm in most centers.

- Technology makes it possible to reduce the duration of sessions

In the past, it was difficult to reduce the duration of the sessions because of patients' poor tolerance. The first effect of the generalization of bicarbonate dialysate was the possibility of reducing the duration of sessions (because of the increase in the hourly rate of UF) as a result of the disappearance of vasodilation caused by acetate dialysate.

Currently, most changes in dialysis generators practically enable better support for a high rate of hourly ultrafiltration necessary to shorten the duration of sessions (isothermal dialysis, isonatric dialysis, blood volume monitoring, development of convective techniques, various UF or sodium profiles, etc.). Sometimes, however, this improvement in dialysis tolerance requires an intake of salt among patients on short dialysis who are often hypertensive.

The evolution of dialysis membranes allows for an extremely rapid purification of urea, and a minimum Kt/V is obtained by increasing the speed of the blood pump to increase K (Urea clearance), making it possible to not increase or even decrease t (dialysis time).

As a result, in the chain of actors in dialysis (doctors, nurses, patients, and managers), all protagonists have a stake in reducing the duration of hemodialysis sessions. With the disappearance of the latest regulatory constraints and quality criteria opposing the reduction in the duration of sessions, the sole conviction of a few nephrologists will not defend for long the benefits of long dialysis, that is, lasting four hours or more.

The danger of short dialysis

The basics of toxicology teach us that a toxicant is all the more dangerous for the subject exposed to it if the level of toxicant is high and the duration of exposure is long. However, when the clearance of the toxin is extremely low or zero, the longer the time interval between two sessions, and the longer the exposure to a high level of the toxin. These theoretical bases have been confirmed in dialysis: patient mortality is higher during the long interdialytic interval of more than two days, imposed by the need to organize dialysis over a seven-day week, including one that is not worked [14].

With high-efficiency dialysis techniques, the purification of small molecules from the plasma sector is extremely rapid. When interdialytic weight gain is moderate, one may wonder what the point of prolonging the session would be since there is nothing more to purify, at least in the plasma sector, the only one accessible to dialysis. The pioneers of dialysis were aware of the danger of excessively effective purification because it causes an osmotic imbalance responsible for a sometimes-fatal postdialytic syndrome [15, 16]. With urea levels before dialysis being much lower than in the 1970s, this phenomenon has become less worrying but still exists [17]. The osmotic imbalance between the intracellular medium and the plasma is quickly corrected by a movement of water toward the intracellular sector before equilibrium is reestablished by the passage of urea between the sectors by trans transporters—urea membranes much less effective than aquaporins.

An exclusive convective technique (isolated ultrafiltration) does not cause osmotic imbalance, nor does it cause thermal imbalance between the dialysate (absent) and the blood. The patient's tolerance to a high rate of ultrafiltration is remarkable, often allowing for treatment of hypertension. Low-reinjection-rate hemofiltration limits osmotic imbalance. This technique was used at the end of the 1970s in patients who could not tolerate hemodialysis sessions. The lack of the possibility of generating the replacement liquid online led to the use of low volumes, which are incompatible with satisfactory purification. Later, the arrival of hemodiafiltration made it possible to correct this drawback at the cost of the return of osmotic and thermal imbalance because of the presence of dialysate.

After a dialysis session, osmotic balance will be achieved with a delay, far from disconnection. It can take up to an hour for water and urea to return to the plasma area. This phenomenon, called the "rebound effect," has been widely documented [18]. The rebound effect is greater in shorter dialysis sessions. During the rebound effect, the patient will feel thirst and will want to compensate for it. They will thus begin their interdialytic period upon leaving the dialysis center, already hyper-hydrated and with a not-insignificant rate of uremic toxins. These phenomena will be all the more important, as the dialysis is quickly effective and short. The increase in the duration of the session makes it possible to reduce the time between two sessions as well as purify, albeit with low efficiency, the toxins released by the intracellular sector after the plasma sector is cleansed.

Despite the shortening of the duration of sessions observed in France between 2012 and 2018, overall dialysis mortality has not deteriorated. There has even been a slight improvement, with the mortality rate dropping from 16.7 to 15.9 per 100 patient-years (Table 1). By way of comparison, the death rate among dialysis patients in the USA is 16.9 per 100 patient-years [19]. It must therefore be noted that despite the physiological considerations described above, the impact of the reduction in the duration of prescribed sessions in 2021 on overall mortality has not been apparent. When these data are stratified, long dialysis treatments support a reduction in the risk of death [5–7]. However, other studies do not support these observations [8].

Regardless of the duration of the session, a high ultrafiltration rate has a strong impact on patient survival. Cardiovascular mortality increases by 71% when the hourly ultrafiltration rate exceeds 13 ml/kg of body weight [20–22]. In the absence of residual diuresis, such an hourly rate of ultra-filtration is generally only achievable with sessions lasting longer than four hours.

Moreover, it appears that the reduction in the duration of the sessions significantly affects patients' comfort, quality of life, and morbidity. Indeed, a major drawback of a short thrice-weekly dialysis is the significant fatigue experienced after the session (postdialysis fatigue), which can last until the next session (interdialytic fatigue), which can be measured [23, 24]. It decreases, or even disappears, in patients treated with long or more frequent dialysis. Thus, the extra time spent on dialysis is more than compensated by the better energy and quality of life in the interdialytic interval [25–29].

Short dialysis, justified in some cases

Incremental dialysis is a concept derived from peritoneal dialysis. After several convergent studies, this notion was integrated in 1997 in the American recommendations NKF/KDOQI [30] for peritoneal dialysis. Incremental dialysis has been defined as a method of addressing impaired renal function to reduce symptoms related to uremia or saltwater overload. The aim was to match the dialysis dose to the residual renal function. Incremental peritoneal dialysis has shown many advantages: less restrictive technique for the patient, more economical for the manager, but also preservation of residual renal function [31, 32] and improvement of patient survival [31, 33, 34].

Incremental dialysis began to be applied to hemodialysis in 1995, initially using a urea-based marker, the solute removal index (SRI) [35]. In fact, it did not appear useful to deliver full-dose dialysis for patients who still had little residual renal function, especially those who were starting hemodialysis. Incremental dialysis has shown the same benefits in hemodialysis as in peritoneal dialysis: preservation of residual renal function [36, 37] and improvement in patient survival [38, 39]. There is therefore an advantage in prescribing shorter and/or less frequent dialysis treatments in patients who still have residual renal function. However, unlike peritoneal dialysis, the development of incremental hemodialysis has not become a prescription standard [39]. Regular assessment of residual kidney function is not standard practice in hemodialysis. In addition, there is no consensus on the method of measuring residual renal function in hemodialysis [40], and above all, there is no validated indicator to determine the minimum duration and frequency of sessions depending on the level of residual renal function.

The reduction in the duration and/or frequency of sessions can be discussed for frail elderly patients, for whom a compromise must be found between quality of life, comfort, and life expectancy. The classic rules of adequacy, particularly with regard to purification, no longer apply when the expected survival expectancy is mainly conditioned by the patient's age or general condition.

CONCLUSION

Apart from the conditions justifying the incremental dialysis, the improvement of results and the tolerance of intermittent dialysis passes mainly by the reduction in the duration of the interdialytic interval, provided of course that purification is sufficient during sessions. This can be achieved by increasing the length of the thrice-weekly dialysis sessions or by increasing the frequency of the sessions.

Many organizational obstacles and patient acceptability do not allow for a strong development of long-term dialysis, but in this period of budgetary constraints, care must be taken to maintain this possibility for patients who already benefit from it and those who could eventually be convinced of its interest. The organization of services should not oppose the occasional possibility of increasing the duration of a session when weight gain is too great.

Daily dialysis is difficult to imagine outside home dialysis, which also allows for long-night dialysis to be carried out. In our experience, patients are equipped at home with conventional generators with water treatment, which allows them to choose their dialysis modality or even adapt it to their activities. Some patients initially treated with daily dialysis for two hours opt for longer dialysis (four hours) every other day, the maximum time between two sessions being thus a little less than two days. The results are thus extremely satisfactory, both in terms of purification, weight control, and blood pressure and quality of life for the patient and interdialytic fatigue.

All that remains is to convince our managers to set up a system allowing dialysis to be performed every other day and patients to adopt this rhythm, or to continue to develop dialysis at home.

The 1970s saw a strong development of home dialysis because it represented the only chance of survival for many. Perhaps we will see a new development of the technique if it becomes the only possibility of quality treatment.

CONFLICT OF INTEREST

The authors declare no conflict of interest for this article.

REFERENCES

1. Lowrie EG, Laird NM, Parker TF, et al. Effect of the hemodialysis prescription of patient morbidity : report from the National Cooperative Dialysis Study. N Eng J Med 1981; 305: 1176-1181.

2. Gotch FA, Sargent JA. A mechanistic analysis of the National Cooperative Dialysis Study (NCDS). Kidney Int 1985; 28 (3): 526–34.

3. Eloot S, Schneditz D, Vanholder R. What can the dialysis physician learn from kinetic modelling beyond Kt/V(urea) ? Nephrol Dial Transplant 2012; 27: 4021-4029

4. Eknoyan G, Beck GJ, Cheung AK, et al. Hemodialysis (HEMO) study Group: effect of dialysis dose and membrane flux in maintenance hemodialysis. N Eng J Med 2002; 347: 2010-2019

5. Nesrallah GE, Lindsay RM, Cuerden MS, et al. Intensive hemodialysis associates with improved survival compared with conventional hemodialysis. J Am Soc Nephrol 2012; 23: 696-705

6. Pauly RP, Gill JS, Rose CL, et al. Survival among nocturnal home hemodialysis patients compared to kidney transplant recipients. Nephrol Dial Transplant 2009; 24:2915-2919

7. Tennankore KK, Kim SJ, Baer HJ, et al. Survival and hospitalization for intensive home hemodialysis compared with kidney transplantation. J Am Soc Nephrol 2014; 25: 2113-2120

8. Rocco MV, Daugidras JT, Greene T, et al.FHN Trial Group: Long-term effects of frequent nocturnal hemodialysis on mortality: the Frequent Hemodialysis Network (FHN) nocturnal trial. Am J Kidney Dis 2015; 66: 459-468

9. Décrets 2002-1198 du 23/09/2002. https://www.legifrance.gouv.fr/jorf/id/JORFTEXT000000780502/

10. Registre REIN 2012. https://www.agence-biomedecine.fr/IMG/pdf/rapport_rein_vdef_2012.pdf

11. Registre REIN 2018. https://www.agence-biomedecine.fr/IMG/pdf/rapport_rein_2018_v2.pdf

12. Landi V. Approche économique de l'hémodialyse quotidienne à domicile (HDQ). Bulletin de la Dialyse à Domicile 2019 ; 3(1) : 37-47

13. Rapport public annuel 2020 – février 2020

Cour des comptes - www.ccomptes.fr - @Courdescomptes

https://www.ccomptes.fr/system/files/2020-02/20200225-03-TomeI-insuffisance-renale-chroniqueterminale.pdf 14. Foley RN, David T. et al. Long Interdialytic Interval and Mortality among Patients Receiving Hemodialysis. N Engl J Med 2011; 365:1099-107.

15. Kennedy AC, Linton AL, Eaton JC. Urea levels in cerebrospinal fluid after haemodialysis. Lancet. 1962;1(7226):410-411.

16. Gottschalk CW, Fellner SK. History of the science of dialysis. Am J Nephrol. 1997;17(3-4):289-298. doi:10.1159/000169116

17. Kirtida Mistry. Dialysis disequilibrium syndrome prevention and management. Int Jour of Nephrology and Renovascular Disease 2019:12 69–77

18. Jean G, Charrat B, Chazot C, et al. Quest for postdialysis urea rebound-equilibrated Kt/V with only intradialytic urea samples. Kidney International, Vol. 56 (1999), pp. 1149–1153

19. Vo DN. Underutilization of home dialysis in the United States: missed opportunities for quality improvement. Bulletin de la Dialyse à Domicile 2018 ; 1(2) : 59-64. <u>https://doi.org/10.25796/bdd.v1i2.46</u>

20. Flythe JE, Kimmel SE, Brunelli SM. Rapid fluid removal during dialysis is associated with cardiovascular morbidity and mortality. Kidney Int 2011; 79: 250-257

21. Flythe JE, Assimon MM, Wenger JB, et al. Ultrafiltration rates and the quality incentive program: proposed measure definitions and their potential dialysis facitily implications. Clin Am Soc Nephrol 2016; 11: 1422-1433

22. Perl J, Dember LM, Bargman JM, et al. The use of a multidimensional measure of dialysis adequacy – moving beyond small solute kinetics. Clin J Am Soc Nephrol 2017; 12: 839-847

23. Sarah J. Ramer and Jennifer S. Scherer. Measuring Fatigue in Hemodialysis Patients. CJASN 2020; 15(11): doi: <u>https://doi.org/10.2215/CJN.14900920</u>

24. Angela JU et al. Validation of a Core Patient-Reported Outcome Measure for Fatigue in Patients Receiving Hemodialysis The SONG-HD Fatigue Instrument CJASN ePress 2020. October 22. doi: 10.2215/ CJN.05880420

25. Henning S. Fatigue While Undergoing Long-Term Hemodialysis. CJASN 2020; 15(11). doi: https://doi.org/10.2215/CJN.14870920

26. Laruelle E. Long nocturnal home hemodialysis: an old therapy brought up to date. Bulletin de la Dialyse à Domicile 2019; 2(1): 11-16 <u>https://bdd.rdplf.org/index.php/bdd/article/view/19113</u>

27. Picault C. Dialyse nocturne à domicile à bas débit de dialysat. Bulletin de la Dialyse à Domicile 2019 ; 2(1) : 33-36 <u>https://bdd.rdplf.org/index.php/bdd/article/view/19143</u>

28. Petitclerc T, AURA-Paris eds 2014. Hemodialyse longue nocturne : Une modalité désormais disponible en région parisienne. <u>https://www.auraparis.org/fr/accueil/travaux/58-hemodialyse-longue-nocturne</u>

29. Koh TJK. Nocturnal hemodialysis : improved quality of life and patient outcomes. Int Jour of Nephrology and Renovascular Disease 2019; 12: 59-68

NKF-DOQI clinical practice guidelines for peritoneal dialysis adequacy. National Kidney Foundation.
Am J Kidney Dis1997 Sep;30(3 Suppl 2):S67-136

31. Sandrini M, Vizzardi V, Valerio F. et al. Incremental peritoneal dialysis: a 10 year single-centre experience. J Nephrol. 2016 Dec;29(6):871-879

32. Borràs Sans M, Chacón Camacho A, Cerdá Vilaplana C. et al. Incremental peritoneal dialysis: Clinical outcomes and residual kidney function preservation. Nefrologia. 2016 May-Jun;36(3):299-303

33. Ankawi GA, Woodcock NI, [...], Blake PG. The Use of Incremental Peritoneal Dialysis in a Large Contemporary Peritoneal Dialysis Program. Can J Kidney Health 2016; 3: 1-7

34. Jeloka T, Sanwaria P, Chaudhari L, Periera A. Ico-Alone: single nocturnal exchange to initiate peritoneal dialysis in patients with residual renal function-Five year, single centre experience. Indian J Nephrol. 2013 Jul;23(4):276-9.

35. Keshaviah P. The Solute Removal Index – a unified basis for comparing disparate therapies. Perit Dial Int 1995; 15: 101-104

36. Liu Y, Zou W, Wu J. et al. Comparison between incremental and thrice-weekly hemodialysis : a systematic review and meta-analysis. Nephrology (Carlton) 2018; Mar 13. <u>https://doi.org/10.1111/nep.13252</u>

37. Termorshuizen F, Dekker FW, Van Manen JG. Et al. Relative contribution of residual renal function and different measures of adequacy to survival in hemodialysis patients : an analysis of the Netherland Cooperative Study on Adequacy of Dialysis (NECOSAD)-2. J Am Soc Nephrol 2004; 15: 1061-1070

38. Wong J, Vilar E, Davenport A, et al. Incremental hemodialysis. Nephrol Dial Transplant 2015; 30: 1639-1648

39. Tattersall J. Residual renal function in incremental dialysis. Clinical Kidney Journal 2018; 11(6): 853-856

40. Mathew AT, Obi Y, Rhee CM, et al. Incremental dialysis for preserving residual kidney function-does one size fit all when initiating dialysis ? Semin Dial 2018; 31: 343-352

41. Hakim RM, Saha S. Dialysis frequency versus dialysis time, that is the question. Kidney Int 2014; 85: 1024-1029

received 2020/11/14 accepted after revision 2021/01/27, published 2021/04/07

Open Access This article is licensed under a Creative Commons Attribution 4.0 International

License, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons license, and indicate if changes were made. The images or other third party material in this article are included in the article's Creative Commons license, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons license and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this license, visit http://creativecommons.org/licenses/by/4.0/.