BIODATA

Nama	:	Anisa
Tempat, Tanggal Lahir	:	Curup, 29 November 2003
Agama	:	Islam
Jenis Kelamin	:	Perempuan
Alamat	:	Sidorejo
Riwayat Pendidikan	:	

1. SDN 02 CURUP TIMUR
2. SMPN 05 REJANG LEBONG
3. SMAN 2 REJANG LEBONG

PERNYATAAN KEASLIAN TULISAN

Saya yang bertanda tangan dibawah ini:

Nama	: Anisa
NIM	: P01720122006
Program Studi	: Diploma Tiga Keperawatan
Institusi	: Poltekkes Kemenkes Bengkulu

Menyatakan dengan sebenarnya bahwa Karya Tulis Ilmiah yang saya tulis ini adalah benar-benar merupakan hasil karya saya sendiri dan bukan merupakan pengambilan alihan tulisan atau pikiran orang lain yang saya akui sebagai hasil tulisan atau pikiran saya sendiri.

Apabila dikemudian hari terbukti atau dapat dibuktikan Karya Tulis Ilmiah ini hasil jiplakan, maka saya bersedia menerima sanksi atas perbuatan saya.

Curup, 5 Agustus 2025

Pembuat Pernyataan

Anisa

P01720122006

Dosen Pembimbing

Dr. Leli Mulyati,SKp,M.Kep.Sp.Kep.MB

NIP.197601172001122002

INFORMED CONSENT

(Persetujuan Menjadi Partisipan)

Saya yang bertanda tangan dibawah ini, menyatakan bahwa saya telah mendapatkan penjelasan secara rinci dan telah mengerti mengenai penelitian yang dilakukan oleh Anisa dengan judul "Asuhan Keperawatan Pada Tn. H Dengan *Chronic Kidney Disease (CKD)* Dengan Implementasi Latihan Intradialitik Untuk Meningkatkan Intoleransi Aktivitas Di Ruang Hemodialisa Rsud Kabupaten Rejang Lebong Tahun 2025 "

Saya memutuskan setuju untuk ikut berpartisipasi pada penelitian secara sukarela tanpa paksaan. Bila selama penelitian ini saya ingin mengundurkan diri, maka saya dapat mengundurkan diri sewaktu waktu tanpa sanksi apapun

Curup, 22. Mei 2025

Saksi	Yang memberi Persetujuan
(...Susanti.....)	(Herno Husda Widianto)

Curup, 22 Mei 2025

Peneliti

(Anisa)

PENJELASAN UNTUK MENGIKUTI PENELITIAN

(PSP)

1. Kami adalah peneliti berasal dari Poltekkes Kemenkes Bengkulu Program Studi Diploma III Keperawatan dengan ini meminta anda untuk berpartisipasi dengan sukarela dalam penelitian berjudul Asuhan Keperawatan pada Tn.H dengan CKD dengan Implementasi Latihan Intradialitik untuk Meningkatkan Intoleransi Aktifitas diruang Hemodialisa RSUD Kabupaten Rejang Lebong Tahun 2025.
2. Tujuan dari penelitian studi kasus ini adalah untuk memperoleh gambaran penerapan asuhan keperawatan pada pasien HD dengan pendekatan proses keperawatan yang dapat memberikan latihan intradialitik untuk meningkatkan intoleransi aktivitas dan kualitas hidup pada pasien HD, sehingga dapat menambah wawasan dan informasi dalam peningkatan intoleransi aktivitas pada pasien HD, penelitian ini akan berlangsung selama 4 hari setelah HD.
3. Prosedur pengambilan data dengan cara wawancara, observasi dan pengisian kuisioner terpimpin dengan menggunakan pedoman wawancara yang akan berlangsung lebih kurang 15-20 menit. Cara ini mungkin menyebabkan ketidaknyamanan tetapi anda tidak perlu khawatir karena penelitian ini untuk kepentingan pengembangan asuhan/pelayanan keperawatan.
4. Keuntungan yang anda peroleh dalam keikutsertaan anda pada penelitian ini adalah anda turut terlibat aktif mengikuti perkembangan asuhan/tindakan yang diberikan.
5. Nama dan jati diri anda beserta seluruh informasi yang saudara sampaikan akan tetap dirahasiakan.
6. Jika saudara membutuhkan informasi sehubungan dengan penelitian ini, silahkan menghubungi peneliti pada no HP: 085609567246

PENELITI

(Anisa)

Kementerian Kesehatan
Poltekkes Bengkulu
Jalan Indragiri No.3 Padang Harapan Bengkulu 38225
(0736) 341212
https://poltekkesbengkulu.ac.id

21 Mei 2025

Nomor : DP.04.03/ F.XXIII.14/ 196 /2025
Lampiran : -
Perihal : **Permohonan Izin Pengambilan Kasus**

Yang Terhormat
Direktur Rumah Sakit Umum Daerah
Kabupaten Rejang Lebong
Di Kelurahan Durian Depun Kecamatan Merigi Kabupaten Kepahiang

Dengan Hormat

Berkenaan dengan Penyelesaian Karya Tulis Ilmiah dalam bentuk laporan kasus bagi mahasiswa Program Studi Keperawatan Program Diploma Tiga Jurusan Keperawatan Poltekkes Kemenkes Bengkulu, Maka bersama ini mohon kesediaan Bapak/Ibu untuk memberikan izin kepada mahasiswa/i kami yang tersebut dibawah ini untuk melakukan Asuhan Keperawatan yang berkaitan dengan judul : ***Asuhan Keperawatan CKD Dengan Implementasi Latihan Intradialitik Untuk Meningkatkan Intoleransi Aktivitas Pada Pasien Hemodialisa Di RSUD Kabupaten Rejang Lebong Tahun 2025***

Adapun nama mahasiswa yang akan melakukan kegiatan tersebut adalah:

Nama : Anisa

Nim : P01720122006

Demikian atas perhatian dan kerja samanya kami ucapkan terima kasih.

Ketua Program Studi Keperawatan
Program Diploma Tiga

Ns.Derison Marsinova Bakara,S.Kep,M.Kep

Tembusan

- Arsip

PEMERINTAH KABUPATEN REJANG LEBONG

RSUD KABUPATEN REJANG LEBONG

Jl. Jalur Dua Kelurahan Durian Depun Kecamatan Merigi Kabupaten Kapahiang
Kode Pos 39371

Nomor : 61 / RSUD – DIKLAT / 2025
Sifat : Biasa
Lampiran : -
Perihal : Keterangan Selesai Pengambilan Kasus

Merigi, 28 Mei 2025
Kepada Yth,
Ka.Prodi Keperawatan Poltekes Bengkulu
Di -
Curup

Sehubungan dengan surat dari Ka.Prodi Keperawatan Program Diploma Tiga Poltekes Kemenkes Bengkulu Nomor: DP.04.03/F.XXXI.14.4/190/2025 tanggal 21 Mei 2025, Perihal Permohonan Izin Pengambilan Kasus atas nama :

Nama	:	**Anisa**
NIM	:	P01720122006
Program Studi	:	D3 Keperawatan
Waktu	:	22 S/d 28 Mei 2025
Judul	:	*Asuhan Keperawatan Chronic Kidney Disease (CKD) Dengan Implementasi Latihan Intradialitik untuk meningkatkan Intoleransi Aktivitas pada Pasien Hemodialisa di RSUD Kabupaten Rejang Lebong Tahun 2025.*
Ruangan	:	*Hemodialisa*

Untuk itu kami kembalikan Mahasiswa yang tersebut diatas dikarenakan telah selesai melaksanakan Pengambilan Kasus pada RSUD Kabupaten Rejang Lebong.

Demikian surat keterangan ini kami buat untuk dapat dipergunakan sebagaimana mestinya.

A.n Plt.Direktur
Kasubbag Umum dan Kepegawaian

PEMERINTAH KABUPATEN REJANG LEBONG RUMAH SAKIT UMUM DAERAH

PENY SUBEKTY S.Kep
Penata TK.I/ III. d
NIP. 198002272003122003

DOKUMENTASI

Tanggal	DOKUMENTASI
Kamis, 22 Mei 2025	   
Senin, 26 Mei 2025	 

	 
Senin, 29 Mei 2025	  

Kamis, 02 Juni 2025	       




STANDAR OPERASIONAL PROSEDUR (SOP) ***INTRADIALYTICE EXERCISE***

A. Keterangan

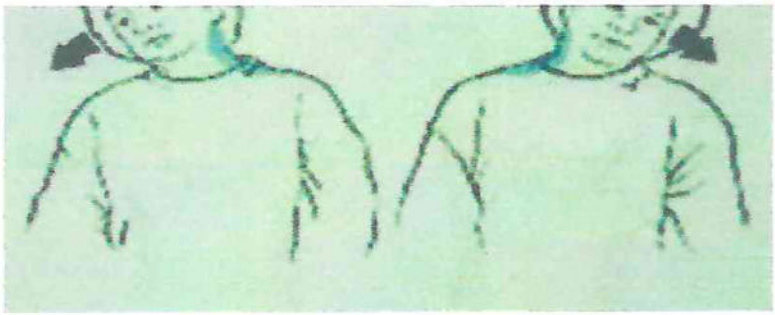
1. Latihan dilakukan 1-2 jam setelah hemodialisa berjalan.
2. Persiapkan alat seperti kursi, dan kain panjang.
3. Intradialytic exercise dilakukan selama 20 menit.
4. Kaji keadaan umum pasien sebelum dan sesudah latihan.
5. Kaji TTV pasien sebelum dan sesudah latihan.
6. Bila terdapat komplikasi hemodialisis maka latihan dihentikan.

B. Prosedur Latihan

1. Flexibility Exercise (Peregangan)

Latihan ini dilakukan dengan meregangkan otot-otot hingga terasa tegangan yang ringan, dan menahannya hingga 10 20 detik, bernafas dalam dan perlahan ketika peregangan dilakukan, lalu keluarkan nafas perlahan saat menahan pada posisi tersebut. Pengulangan sedikitnya dilakukan sebanyak 3 kali.

a. Peregangan Leher



Gambar 1. Peregangan leher

keterangan gambar 1:

1. Duduk atau berdiri tegak, pandangan lurus kedepan.
2. Perlahan dekatkan telinga kanan kearah bahu kanan. Putar kepala ke arah belakang dan dekatkan telinga kiri kebahu kiri.
3. Dekatkan dagu ke dada dan putar perlahan dagu kearah sepanjang dada sehingga telinga kiri menyentuh bahu kiri.
4. Tegakkan kembali dagu hingga pandangan lurus ke depan.

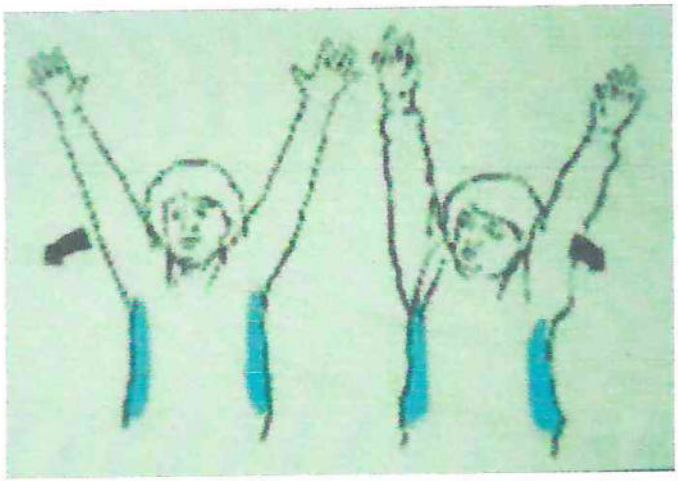
b. Peregangan lengan dan tangan

Gambar 2. Peegangan lengan dan tangan

Keterangan gambar 2 :

1. Duduk atau berdiri tegak.
2. Luruskan lengan ke depan setinggi bahu.
3. Regangkan seluruh jari lalu buat kepalan tangan dan lepaskan lagi Lengan tetap lurus kedepan lalu putaran dipergelangan tangan pertama searah jarum jam kemudian berlawanan arah jarum jam.

c. Peregangan pinggang



Gambar 3. Peregangan pinggang

Keterangan gambar 3:

1. Berdiri atau duduk tegak
2. Letakkan lengan di atas kepala, lalu jatuhkan lengan sebelah kanan dan rasakan tarikan, lalu tegak kembali
3. Lakukan yang sama pada lengan kiri

d. Peregangan dada dan punggung belakang

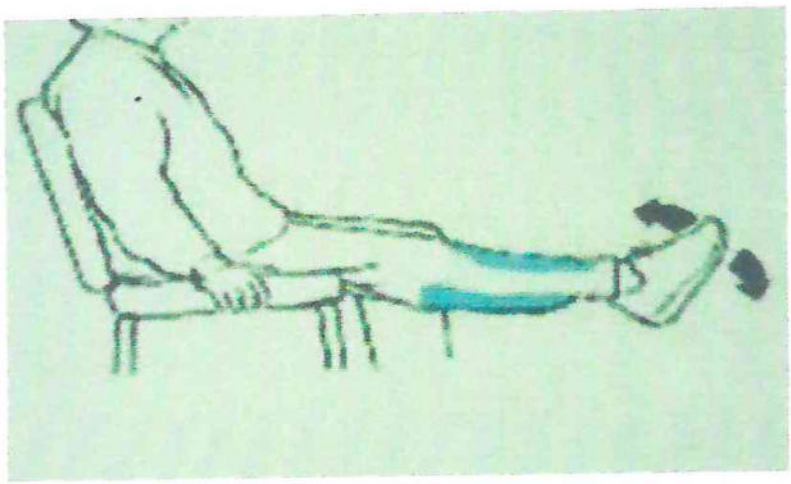
Gambar 4. Peregangan dada dan punggung belakang

Keterangan gambar 4:

1. Berdiri atau duduk tegak
2. Letakkan tangan dibahu dengan siku diluar

3. Buat lingkaran dgn siku pertama ke depan lalu ke belakang
4. Stop membuat lingkaran lalu buat siku berdekatan di depan dada.
5. Buka kembali siku dan lalu regangkan rasakan tekanan didada.

e. Peregangan kaki



gambar 5. Peregangan kaki

keterangan gambar 5:

1. Duduk tegak dengan kaki dilantai, berpegangan pada kursi .
2. Perlahan angkat kaki kanan sampai lurus didepan
3. Kemudian perhatikan jempol kaki, lalu gerakkan kedepan dan ke belakang.
4. Gerakkan tumit memutar pertama ke kanan lalu ke kiri. Letakkan kaki kanan ke lantai dan lakukan juga pada kaki kiri.

LEMBAR KUISIONER KUALITAS HIDUP WHOQOL-BREF (sebelum)

Inital nama : Tn. H

Jenis kelamin : laki-laki

Usia : 48 tahun

Petunjuk pengisian :

1. Pertanyaan berikut ini menyangkut perasaan anda terhadap kualitas hidup dan hal hal lain dalam hidup anda

2. Bacalah setiap pertanyaan dengan teliti

3. Pilih jawaban yang menurut anda paling sesuai dengan kondisi anda

4. Beri tanda cek (✓)pada kolom yang tersedia di setiap pertanyaan .

Pilihlah jawaban yang menrut bapak/ibu paling sesuai ,jika bapak /ibu tidak yakin tentang jawaban yang akan diberikan terhadap pertanyaan yang telah diajukan,pikiran utama yang muncul pada benak bapak/ibu seringkali merupakan jawaban yang terbaik.

A. Camkanlah dalam pikiran segala standar hidup,harapan,kesenangan dan perhatian .

No	Pertanyaan	Sangat buruk	buruk	Biasa saja	baik	Sangat baik	
1.	Bagaimana menurut bapak/ibu kualitas hidup bapak/ibu ?		✓				2
2.	Seberapa puas bapak /ibu terhadap kesehatan bapak atau ibu ?		✓				2

B. seberapa sering mengalami hal-hal berikut?

No	Pertanyaan	Tidak sama sekali	Sedikit	Dalam jumlah sedang	Sangat sering	Dalam jumlah berlebihan	
3.	Seberapa jauh rasa sakit fisik bapak/ibu mencegah bapak/ibu dalam beraktivitas sesuai kebutuhan bapak/ibu				✓		2
4.	Seberapa sering bapak/ibu membutuhkan terapi medis untuk dapat berfungsi dalam kehidupan sehari-hari bapak/ibu?				✓		2
5.	Sebearapa jauh bapak/ibu menikmati hidup bapak ibu?	✓					1
6.	Seberapa jauh bapak/ibu merasa hidup bapak/ibu berarti?	✓					1
7.	Seberapa jauh bapak/ibu mampu berkomunikasi?		✓				2
8.	Secara umum, seberapa aman bapak/ibu rasakan dalam kehidupan bapak/ibu sehari-hari?	✓					1
9.	Seberapa sehat lingkungan dimana bapak/ibu tinggal (berkaitan dengan sarana dan prasarana)?			✓			3

C. seberapa penuh bapak /ibu alami hal-hal berikut ?

No	Pertanyaan	Tidak sama sekali	Sedikit	Sedang	Sering kali	Dialami sepenuhnya	
10.	Apakah bapak/ibu memiliki vitalitas yang cukup unntuk beraktivitas sehari hari?	✓					1
11.	Apakah bapak/ibu dapat menerima penampilan tubuh bapak/ibu ?	✓					1
12.	Apakah bapak/ibu memiliki cukup uang untuk memenuhi kebutuhan hidup?		✓				2
13.	Seberapa jauh ketersediaan informasi bagi kehidupan bapak/ibu dari hari ke hari?	✓					1
14.	Seberapa sering bapak/ibu memiliki kesempatan untuk bersenang senang 7berkreasi?	✓					1
15.	Seberapa baik kemampuan bapak/ibu dalam bergaul?		✓				2

No	Pertanyaan	Sangat tidak memuaskan	Tidak memuaskan	Biasa saja	Memuaskan	Sangat memuaskan	
16.	Seberapa puaskah bapak/ibu dengan tidur bapak/ibu?	✓					1
17.	Seberapa puaskah bapak/ibu dengan kemampuan bapak/ibu untuk menampilkan aktivitas kehidupan bapak/ibu sehari-hari?	✓					1
18.	Seberapa puaskah bapak/ibu dengan kemampuan bapak/ibu untuk bekerja?	✓					1
19.	Seberapa puaskah bapak/ibu terhadap diri sendiri?	✓					1
20.	Seberapa puaskah bapak/ibu dengan hubungan personal/sosial bapak/ibu?		✓				2
21.	Seberapa puaskah bapak/ibu dengan kehidupan seksual bapak/ibu?	✓					1
22.	Seberapa puaskah bapak/ibu dengan dukungan yang di perleh dari teman ?		✓				2

23.	Seberapa puaskah bapak/ibu dengan kondisi tempat tinggal bapak/ibu saat ini?		✓			2
24.	Seberapa puaskah bapak/ibu dengan akses pada pelayanan kesehatan ?		✓			2
25.	Seberapa puaskah bapak/ibu dengan transportasi yang ibu jalani ?	✓				1

D. seberapa sering bapak/ibu merasakan atau mengalami hal hal berikut ?

No	Pertanyaan	Tidak pernah	Jarang	Cukup sering	Sangat sering	Selalu	
26.	Seberapa sering bapak/ibu memiliki perasaan negatif seperti kesepian,putus asa,,cemas, dan depresi?					✓	1

Total : 39

Keterangan :

1 = sangat buruk

2 = buruk

3 = biasa saja

4 = baik

5 = sangat baik

Interpretasi Skor :

0-50 = kualitas hidup buruuk

51- 100 = kualitas hidup baik

LEMBAR KUISIONER KUALITAS HIDUP WHOQOL-BREF (sesudah)

Inital nama : Tn.H

Jenis kelamin : laki - laki

Usia : 78 tahun

Petunjuk pengisian :

1. Pertanyaan berikut ini menyangkut perasaan anda terhadap kualitas hidup dan hal hal lain dalam hidup anda

2. Bacalah setiap pertanyaan dengan teliti

3. Pilih jawaban yang menurut anda paling sesuai dengan kondisi anda

4. Beri tanda cek (✓)pada kolom yang tersedia di setiap pertanyaan .

Pilihlah jawaban yang menrut bapak/ibu paling sesuai ,jika bapak /ibu tidak yakin tentang jawaban yang akan diberikan terhadap pertanyaan yang telah diajukan,pikiran utama yang muncul pada benak bapak/ibu seringkali merupakan jawaban yang terbaik.

A. Camkanlah dalam pikiran segala standar hidup,harapan,kesenangan dan perhatian .

No	Pertanyaan	Sangat buruk	buruk	Biasa saja	baik	Sangat baik
1.	Bagaimana menurut bapak/ibu kualitas hidup bapak/ibu ?				✓	
2.	Seberapa puas bapak /ibu terhadap kesehatan bapak atau ibu ?				✓	

B. seberapa sering mengalami hal-hal berikut?

No	Pertanyaan	Tidak sama sekali	Sedikit	Dalam jumlah sedang	Sangat sering	Dalam jumlah berlebihan
3.	Seberapa jauh rasa sakit fisik bapak/ibu mencegah bapak/ibu dalam beraktivitas sesuai kebutuhan bapak/ibu			✓		
4.	Seberapa sering bapak/ibu membutuhkan terapi medis untuk dapat berfungsi dalam kehidupan sehari-hari bapak/ibu?			✓		
5.	Sebearapa jauh bapak/ibu menikmati hidup bapak ibu?		✓			
6.	Seberapa jauh bapak/ibu merasa hidup bapak/ibu berarti?		✓			
7.	Seberapa jauh bapak/ibu mampu berkomunikasi?				✓	
8.	Secara umum, seberapa aman bapak/ibu rasakan dalam kehidupan bapak/ibu sehari-hari?		✓			
9.	Seberapa sehat lingkungan dimana bapak/ibu tinggal (berkaitan dengan sarana dan prasarana)?			✓		

C. seberapa penuh bapak /ibu alami hal-hal berikut ?

No	Pertanyaan	Tidak sama sekali	Sedikit	Sedang	Sering kali	Dialami sepenuhnya
10.	Apakah bapak/ibu memiliki vitalitas yang cukup unntuk beraktivitas sehari hari?			✓		
11.	Apakah bapak/ibu dapat menerima penampilan tubuh bapak/ibu ?			✓		
12.	Apakah bapak/ibu memiliki cukup uang untuk memenuhi kebutuhan hidup?		✓			
13.	Seberapa jauh ketersediaan informasi bagi kehidupan bapak/ibu dari hari ke hari?			✓		
14.	Seberapa sering bapak/ibu memiliki kesempatan untuk bersenang senang /berkreasi?	✓				
15.	Seberapa baik kemampuan bapak/ibu dalam bergaul?			✓		

No	Pertanyaan	Sangat tidak memuaskan	Tidak memuaskan	Biasa saja	Memuaskan	Sangat memuaskan
16.	Seberapa puaskah bapak/ibu dengan tidur bapak/ibu?				✓	
17.	Seberapa puaskah bapak/ibu dengan kemampuan bapak/ibu untuk menampilkan aktivitas kehidupan bapak/ibu sehari-hari?				✓	
18.	Seberapa puaskah bapak/ibu dengan kemampuan bapak/ibu untuk bekerja?		✓			
19.	Seberapa puaskah bapak/ibu terhadap diri sendiri?			✓		
20.	Seberapa puaskah bapak/ibu dengan hubungan personal/sosial bapak/ibu?			✓		
21.	Seberapa puaskah bapak/ibu dengan kehidupan seksual bapak/ibu?		✓			
22.	Seberapa puaskah bapak/ibu dengan dukungan yang di perleh dari teman ?			✓		

23.	Seberapa puaskah bapak/ibu dengan kondisi tempat tinggal bapak/ibu saat ini?			✓		
24.	Seberapa puaskah bapak/ibu dengan akses pada pelayanan kesehatan ?			✓		
25.	Seberapa puaskah bapak/ibu dengan transportasi yang ibu jalani ?	✓				

D. seberapa sering bapak/ibu merasakan atau mengalami hal hal berikut ?

No	Pertanyaan	Tidak pernah	Jarang	Cukup sering	Sangat sering	Selalu
26.	Seberapa sering bapak/ibu memiliki perasaan negatif seperti kesepian,putus asa,,cemas, dan depresi?		✓			

Total : 72.

Keterangan :

1 = sangat buruk

2 = buruk

3 = biasa saja

4 = baik

5 = sangat baik

Interpretasi Skor :

0-50 = kualitas hidup buruuk

51- 100 = kualitas hidup baik

Lembar Pemantauan Intake Output Cairan

Tanggal : 26 Mei 2025 BB : 67,8 Kg							Tanggal : 29 Mei 2025 BB : 67,6 kg						Tanggal : 2 juni 2025 BB : 65,5 Kg					
Waktu	**Cairan Masuk**		**Cairan Keluar**				**Cairan Masuk**		**Cairan Keluar**				**Cairan Masuk**		**Cairan Keluar**			
	Minum	Makan	Muntah	Urin	BAB	Ket	Minum	Makan	Muntah	Urin	BAB	Ket	Minum	Makan	Muntah	Urin	BAB	Ket
01.00																		
02.00																		
03.00																		
04.00																		
05.00																		
06.00																		
07.00																		
08.00							350 ml						300 ml					
09.00																		
10.00																		
11.00													100 ml					
12.00																		
13.00							300 ml											
14.00	350 ml												300 ml					
15.00																		
16.00							200 ml											
17.00	300 ml																	
18.00																70 ml		

19.00				50 ml			250 ml						200 ml					
20.00	350 ml																	
21.00										60 ml								
22.00	200 ml												200 ml					
23.00																		
24.00																		
Total 24 jam	1.200 ml						1100 ml						1100 ml					

HASIL BALANCE CAIRAN

HARI/TANGGAL	INTAKE	OUTPPUT
Senin 26 Mei 2025 BB = 67,4 Kg	Minum (24 jam) : 1.200 ml Makan : Hasil intake = 1.200 ml	Urine (24 jam) : 50 ml IWL (24 jam) : 1014 ml Muntah : - BAB : - Hasil output = 1064 ml
Balance cairan 24 jam = Intake – Output (1.200 ml - 1064 ml = positif 136 ml)		
Kamis 29 Mei 2025 BB = 67,2 Kg	Minum : 1100 ml Makan : - Hasil intake = 1100 ml	Urin : 60 ml IWL (24 jam) : 1.008 ml BAB : - Muntah :- Hasil output = 1068 ml
Balance cairan 24 jam = Intake – Output (1100 ml - 1068 ml = positif 32 ml)		
Senin 02 juni 2025 BB = 67 Kg	Minum : 1100 ml Makan : - Hasil intake = 1100 ml	Urin : 70 ml IWL (24 jam) : 1.005 ml Muntah : - BAB : - Hasil output = 1075 ml
Balance cairan 24 jam = intake – output (1100 ml - 1075 ml = positif 25 ml)		

LEMBAR OBSERVASI
LATIHAN INTRADIALITIK

No	Hari/tanggal	Kegiatan yang dilakukan	Sebelum dilakukan tindakan	Setelah dilakukan tindakan
1.	Kamis 22 mei 2025	Pertemuan 1: 1. Mengukur kualitas hidup dengan menggunakan kuisioner	Score dibawah 50	
2.	Kamis 22 mei 2025	2. Mengukur TTV a. TD	200/110 mHg	204/114mmHg
		b. HR	88 x/menit	93x/menit
		c. RR	20x/menit	24x/menit
		d. SPO2	98%	98%
		e. T	36.8 °C	37,2 °C
2.	senin 25 mei 2025	Pertemuan 2 : 1. Mengukur TTV 1. TD	190/100 mHg 75 x/menit	200/104 mmHg
		2. HR	20 x/menit	85x/menit
		3. RR	98%	23x/menit
		4. SPO2	36,6 °C	99%
		5. T		36,9 °C
3.	Kamis 29 mei 2025	Pertemuan 3: a. Mengukur TTV a. TD	190/100 mHg 85x/menit	200/110 mmHg
		b. HR	21x/menit	92x/menit
		c. RR	98%	23x/menit
		d. SPO2	36,4 ° C	98%
		e. T		36,8 °C
4.	senin 02 juni 2025	Pertemuan 4: a. Mengukur TTV 1. TD	180/100 mHg 85x/menit	190/100 mmHg
		2. HR	21x/menit	93x/menit
		3. RR	97%	23x/menit
		4. SPO2	36,4 ° C	98%
		5. T		36,7 ° C
		b. Mengukur kualitas hidup dengan menggunakan kuisioner	Score diatas 50	

LEMBAR BIMBINGAN KTI

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JUDUL : Asuhan keperawatan pada Tn.H dengan *Chronik Kidney Disease* (CKD) dengan implementasi latihan intradialitik untuk meningkatkan intoleransi aktivitas diruang Hemodialisa di RSUD Rejang Lebong tahun 2025

No	Hari/Tgl	Topik	Saran Pembimbing	Paraf Pembimbing
1.	Rabu / 01 januari 2025	Konsul judul	Acc judul latihan intadialitik	
2.	Kamis / 02 januari 2025	Konsul Bab 1	1.Mencari jurnal tambahan atau pendukung 2.Menambahkan kuisioner kualitas hidup	
3.	Jumat / 03 januari 2025	Konsul Bab 1	1.Memperbaiki latar belakang 2.Mencari WHO terbaru 3.Latar belakang masukan jurnal 4.Penulisan huruf diperbaiki 5.Manambahkan tujuan khusus	
4.	Senin / 06 januari 2025	Konsul Bab 2	1.Memperbaiki konsep askep 2.Memperbaiki margins	
5.	Jumat / 10 januari 2025	Konsul bab 3	1.Menambahkan SOP dan kuisioner 2. Paham isi jurnal	

6.	Kamis / 20 februari 2025	Revisi Bab 1 Revisi Bab 2 Revisi Bab 3	1.Pebaiki penulisan cover 2.Perbaiki daftar isi 3.Memperbaiki tujuan penelitian 1.Memperbaiki manifestasi klinik 2.Memperbaiki penulisan penulis 3.Memperbaiki evideance based latihan intadialtik 4.Menambahkan latihan intradialitik ke dalam intoleransi aktivitas 1.Menambahakn kriteria inklusi 2.Memperbaiki definisi oprasional dan pengumpulan data	
7.	Jumat /21 Februari 2025	ACC proposal	1.Membuat lembar observasi	
8.	Kamis/ 18 Mei 2025	Konsultasi bab 4	1.menambahkan riwayat HD pasien 2.melengkapi dan menambahkan derajat edema 3.BB sebelum dan sesudah HD diperbaiki 4.menghitung balance cairan 5.menambahkan intervensi apa saja yang dilanjutkan	
9.	Selasa / 24 Mei 2025	Revisi bab 4 dan konsultasi bab 5	1.memperbaiki derajat edema 2.menambahkan implementasi pengisian kuisioner pertemuan petama dan terakhir di pembahasan	
10.	Kamis / 26 Mei 2025	Revisi bab 5	1.menambahkan hasil kuisioner pada pertemuan pertama pada kesimpulan pengkajian bab 5 2.menambahkan hasil kuisioner pada pertemuan ke 4 setelah latihan intradialitik pada kesimpulan evaluasi bab 5	
11.	Jumat / 27 Juni 2025	Revisi bab 5	1.membandingkan hasil dari penilaian kuisoner kualitas hidup	

			pada pertemuan petama dan terakhir pada pembahasan bab 4	
12.	Senin / 30 Juni 2025	ACC KTI	1.seminar hasil pada rabu 03 Juli 2025	

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No	Hari/Tgl	Topik	Saran Pembimbing	Paraf Pembimbing
1.	Rabu / 01 januari 2025	Konsul judul	Acc judul latihan intadialitik	
2.	Kamis / 02 januari 2025	Konsul Bab 1	1.Mencari jurnal tambahan atau pendukung 2.Menambahkan kuisioner kualitas hidup	
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			pada pertemuan petama dan terakhir pada pembahasan bab 4	
12.	Senin / 30 Juni 2025	ACC KTI	1.seminar hasil pada rabu 03 Juli 2025	

ASUHAN KEPERAWATAN CHRONIC KIDNEY DISEASE (CKD) PADA TN. H DENGAN IMPLEMENTASI LATIHAN INTRADIALITIK UNTUK MENINGKATKAN INTOLERANSI AKTIVITAS DI RUANG HEMODIALISA RSUD KABUPATEN REJANG LEBONG TAHUN 2025

By Anisa (Poltekkes Kemenkes Bengkulu)

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4.1 Pembahasan

Pada bab pembahasan penulis akan membandingkan antara teori asuhan keperawatan *Chronic Kidney Disease* (CKD) dengan praktik asuhan keperawatan dengan menggunakan proses keperawatan yaitu pengkajian, perumusan diagnosa, rencana keperawatan, implementasi keperawatan dan evaluasi keperawatan. Sehingga dari proses keperawatan tersebut dapat diambil kesimpulan pemecahan masalah serta dapat digunakan sebagai tindak lanjut dalam penerapan asuhan keperawatan yang efektif dan efisien khususnya pada studi kasus asuhan keperawatan pada Tn.H dengan penyakit *Chronic Kidney Disease* (CKD) di ruang Hemodialisa RSUD Kabupaten Rejang Lebong.

4.1.1 Pengkajian

Pengkajian merupakan dasar utama dan tahap awal dalam sebuah proses keperawatan. Tahap pengkajian ini terdiri dari pengumpulan data dan masalah yang dialami oleh pasien. Pada tanggal 22 Mei 2025 dilakukan pengkajian pada Tn.H dengan penyakit CKD, dalam proses mengumpulkan data penulis menggunakan beberapa metode yaitu metode wawancara dengan pasien dan keluarga pasien, mengobservasi keadaan pasien dengan melakukan pemeriksaan fisik pada setiap sistem tubuh secara sistematis agar bisa didapatkan hasil yang akurat dan pemerikasan kekuatan otot . Selain itu dilakukan juga pengisian kuisiner tentang kualitas hidup serta catatan perawatan dan catatan

medis juga sangat diperlukan untuk melihat data penunjang sehingga semua data dapat terlengkapi.

Pada Tn.H dengan *chronic kidney disease* (CKD) dilakukan pengkajian didapatkan hasil pasien mengatakan susah beraktivitas karena merasakan lemah, keram pada tangan dan kaki yang sulit digerakan karena setelah melaksanakan HD. Menurut teori Lev Vygotsky tanda dan gejala intoleransi aktivitas yaitu mengeluh lelah atau cepat lelah saat beraktivitas,sesak nafas saat beraktivitas , merasa tidak nyaman saat beraktivitas ,merasa lemah dan lemas ,gangguan tidur , jantung berdebar debar ,nafsu makan menurun

Intoleransi aktivitas adalah ketidakcukupan energi untuk melakukan aktivitas sehari hari atau yang diinginkan dengan gejala utama sesak dan kelelahan saat aktivitas(Imardiani,2020). Asumsi peneliti pada Tn.H ada kesenjangan dengan teori dimana Tn.H didapattkan tanda dan gejala merasa lemah dan keram pada tangan dan kaki yang sulit digerakan untuk melakukan aktivitas setelah HD

4.1.2 Diagnosa Keperawatan

Setelah dilakukan pengumpulan data melalui hasil pengkajian selanjutnya penulis menganalisis data yang didapatkan dan mengidentifikasi prioritas masalah pada pasien dengan CKD berdasarkan teori Nurarif (2015) dan Standar Diagnosa Keperawatan Indonesia (SDKI) (2016) yaitu sebagai berikut :

a. Hipervolemia b.d gangguan mekanisme regulasi

b. Gangguan integritas kulit b.d kelebihan volume cairan

c. Intoleransi aktifitas b.d kelemahan

d. Nausea b.d gangguan biokimiawi (uremia)

e. Defisit pengetahuan b.d kurang terpapar informasi

f. Resiko perfusi renal tidak efektif d.d disfungsi ginjal

g. Resiko penurunan curah jantung d.d perubahan frekuensi jantung

Berdasarkan data yang didapatkan diagnosa keperawatan yang ditemukan dan dapat ditegakkan pada Tn.H yaitu :

a. Hipervolemia berhubungan dengan gangguan mekanisme regulasi, diagnosa keperawatan ini ditegakkan karena berdasarkan data yang didapatkan dari keluhan pasien mengalami pembengkakan atau edema pada kedua kaki dan mengalami peningkatan berat badan yang cukup tajam dalam waktu yang dekat, selain itu pasien juga mengalami penurunan output urin.

b. Gangguan integritas kulit berhubungan dengan kelebihan volume cairan, diagnosa keperawatan ini dapat ditegakkan karena berdasarkan data yang didapatkan dari keluhan pasien yaitu pasien mengeluh kulit terasa kering saat sesudah Hemodialisa , tekstur kulit yang buruk serta kemerahan dan tampak pucat

c. Intoleransi aktivitas berhubungan dengan kelemahan, diagnosa ini ditegakkan oleh penulis karena berdasarkan data yang didapatkan dari hasil pengkajian klien mengatakan klien merasa lemas tidak bertenaga dan merasakan keram pada pada kedua tangan dan kaki

yang sulit di gerakan untuk aktivitas

Ada beberapa diagnosa keperawatan diteori yang tidak ditegakkan oleh penulis dikarenakan beberapa data pendukung tidak ditemukan saat pengkajian untuk mengangkat diagnosa tersebut.

4.1.3 Intervensi Keperawatan

Langkah awal dalam pembuatan rencana keperawatan yaitu diagnosa,tujuan dan sasaran,kriteria dan evaluasi serta intervensi dan tindakan keperawatan .Tidak semua rencana tindakan keperawatan dapat diterapkan karena penulis menyesuaikan dengan kondisi klien dan sarana pada RSUD Curup Kabupaten Rejang Lebong. Perencanaan ini bersumber dari SIKI DPP PPNI (2018),dimana bertjuan untuk meningkatkan intoleransi aktivitas pada pasien *chronic kidney disease* (CKD) dengan tindakan latihan intradialitik

4.1.4 Implementasi Keperawatan

Perencanaan keperawatan yang telah disusun diwujudkan melalui praktik atau implementasi keperawatan. Pelaksanaan tindakan yang telah direncanakan dilakukan secara mandiri dan bekerja sama dengan keluarga pasien. Tidak semua rencana tindakan dapat dilakukan oleh penulis sendiri, penulis juga bekerja sama dengan keluarga pasien dalam memantau intake output cairan pada pasien.

Tindakan keperawatan pada diagnosa intoleransi aktivitas berhubungan dengan kelemahan adalah mengidentifikasikan gangguan fungsi tubuh yang mengakibatkan kelelahan, memonitor kelelahan fisik

dan emosional dan melakukan latihan intradialitik dimana latihan ini dapat meningkatkan kekuatan otot pada pasien Hemodialisa dan menganjurkan melakukan aktivitas latihan intradialtik secara bertahap.

Kegiatan dengan manajemen hipervolemia adalah menimbang berat badan sebelum dan sesudah hemodialisa dan latihan intradialitik untuk meningkatkan intoleransi aktivitas dan kualitas hidup pada pasien hemodialisa dilakukan selama 3 hari dan dihari keempat dilakukan evaluasi sesudah pasien melakukan HD dan mengisi kuisioner kualitas hidup

Tindakan keperawatan pada diagnosa gangguan integritas kulit berhubungan dengan kelebihan volume cairan yaitu identifikasi dampak kulit kering, monitor jaringan kulit, monitor keelastisan kulit, anjurkan menggunakan pelembab contohnya lotion anjurkan meningkatkan asupan nutrisi dan menghindari paparan suhu ekstreme.

Pada implementasi hari ke dua penulis melakukan implementasi yaitu dilakukan pengukuran pada jam yang sama saat pasien melakukan penimbangan berat badan di hari pertama. Saat melakukan pengukuran penulis menimbang berat badan pasien, setelah itu mengevaluasi pemantauan lembar intake dan output cairan yang ditinggalkan dengan keluarga pasien dan mengingatkan kembali pada pasien cara manajemen cairan dengan benar dan kembali mengajarkan latihan intradialitik untuk pada pasien karena pasien mengatakan keram pada kedua kaki dan tangan sehingga dapat meningkatkan kekuatan

otot.

Selanjutnya implementasi dihari ke tiga penulis juga melakukan penimbangan berat badan serta mengevaluasi lembar intake output cairan yang penulis minta keluarga dan pasien untuk mengisinya selama 24 jam selama 4 hari HD dan melakukan latihan intradialitik setelah dilakukan hemodialisa

Pada hari keempat penulis hanya mengevaluasi dengan menimbang berat badan pasien serta menghitung balance cairan melalui lembar pemantauan intake dan output dan mengevaluasi perkembangan intoleransi aktivitas dengan melakukan latihan intradilitik dan menilai kekuatan otot dan intoleransi aktivitas meningkat yang terakhir dan melakukan pengisian kuisioner ahir kualitas hidup.

Pada hari ke empat setelah dilakukan terapi latihan intradialitik selama 10-15 menit klien mengatakan sudah lebih baik, keram pada tangan dan kaki sudah berkurang sudah bisa melakukan aktivitas sehari hari kelemahan menurun dan klien merasa tubuh lebih bersemangat ,edema menurun .

Menurut Ammirati (2019) setelah dilakukan terapi latihan intradialitik intoleransi aktivitas meningkat pada semua yang menjalan kan HD yang pada awalnya tidak normal namun setelah dilakukan terapi masalah pada intoleransi aktivtas menjadi meningkat.Asumsi penulis terdapat kesamaan antara teori dan penelitian yang sudah dilakukan dimana terdapat kesamaan peningkatan intoleransi aktivitas.

4.1.5 Evaluasi Keperawatan

Setelah dilakukan tindakan keperawatan selama 4 hari setelah HD dilaksaanakan dan dihari ke- 4 dievaluasi kembali, dan melakukan pengisian kuisioner kualitas hidup kembali dan didapatkan skor meningkat dari sebelumnya , dari 3 diagnosa keperawatan yang ditegakkan ada 1 diagnosa keperawatan yang sudah teratasi pada tanggal 28 Mei 2025 . Setelah dilakukan evaluasi keperawatan pada Tn.H dengan diagnosa medis CKD terdapat 3 diagnosa teratasi diantaranya :

Gangguan integritas kulit berhubungan dengan kelebihan volume cairan teratasi setelah 3 hari implementasi yaitu ditanggal 29 Mei 2025 dengan data subjektif klien mengatakan kulit terasa kering sudah berkurang, serta nafsu makan mulai membaik dan benar.

Intoleransi aktivitas berhubungan dengan kelemahan ketidakcukupan energi secara fisiologis maupun fsikologis untuk meneruskan atau menyelesaikan masalah aktivitas sehari hari.penulis tidak memprioritaskan masalah tersebut karena tidak mengancam kehidupan pasien. Tapi jika tidak ditegakan klien tidak dapat mandiri dalam menyelesaikan aktivitas . masalah intoleransi aktivitas teratasi setelah 4 hari implementasi yaitu ditanggal 02 juli 2025 dengan melakukan latihan intradialitk setelah pasien hemodialisa dengan data subjektif klien mengatakan kaki dan tangan klien sudah tidak keram lagi setelah latihan inradialitik dilakukan. Dengan data objektif

mengevaluasi kemampuan melakukan aktivitas sehari hari meningkat dan kekuatan otot pada ekstremitas atas dan bawah meningkat dan kelemahan menurun.

Hipervolemia berhubungan dengan gangguan mekanisme regulasi dievaluasi di hari ke-4 sebelum pasien melakukan HD untuk melihat dan mengevaluasi berat badan antar post HD dan pre HD selanjutnya, dengan hasil subjektif klien mengatakan bengkak di kakinya sudah berkurang dan setelah dilakukan penimbangan berat badan terjadi penurunan berat badan yang cukup signifikan.

Pengisian kuisioner kualitas hidup dilakukan ketika pertama kali pertemuan dan sebelum melakukan latihan intradialitik. Pengisian kuisioner pertama dilakukan kepada pasien sebelum latihan intradialitik mendapatkan skor 39 yang dimana merupakan kualitas hidup yang buruk. Setelah dilakukan latihan intradialitik kepada pasien selama 4 kali pertemuan setelah HD pasien kembali mengisi kuisioner kualitas hidup dengan hasil skor 72 dimana dengan kualitas hidup membaik.jadı perbandingan pengisian kuisioner kualitas hidup pertama dan pengisian kuisioner kualitas hidup setelah dilakukan latihan intradialitik meningkat senilai 28 dengan demikian dengan dilakukannya latihan intradialitik dapat meningkatkan kualitas hidup seseorang.

Menurut Ammirati (2019) setelah dilakukan terapi latihan intradialitik intoleransi aktivitas pada pasien yang menjalani HD menjadi meningkat yang awalnya tidak bisa melakukan kegiatan sehari hari bisa melakukan kegiatan sehari hari dengan cara bertahap.Asumsi

penulis terdapat kesamaan pada teori dan penelitian yang dilakukan pada Tn.H dimana terdapat penurunan kelemahan dan kemampuan melakukan aktivitas meningkat setelah dilakukan terapi selama 4 kali dalm 2 minggu.

4.2 Keterbatasan Penelitian

Keterbatasan dalam penelitian ini adalah pada saat melakukan latihan intradialitik penulis menggunakan metode yang menujukan gerakan lewat booklet, pada saat pasien melakukan latihan intradialitik setelah HD penulis menggunakan SOP sudah di print mengakibatkan pasien susah untuk mengikuti gerakan yang diajarkan . Keterbatasan penelitian yang kedua yaitu lembar pemantauan intake output cairan ditinggalkan pada pasien dan keluarga di rumah, dalam pencatatan lembar intake output pun dilakukan oleh pasien dan keluarga secara mandiri dikarenakan keterbatasan penulis yang tidak mampu memantau sendiri seberapa banyak cairan masuk ke dalam tubuh pasien secara detail seperti seberapa banyak air yang diminum, bagaimana ukuran gelas yang digunakan sehingga hasil intake output cairan dan penimbangan berat badan bertolak belakang atau dapat dikatakan adanya kesenjangan data, dimana pada hasil balance cairan hasilnya positif sedangkan pada penimbangan berat badan hasilnya mengalami penurunan berat badan yang signifikan.

ASUHAN KEPERAWATAN CHRONIC KIDNEY DISEASE (CKD) PADA TN. H DENGAN IMPLEMENTASI LATIHAN INTRADIALITIK UNTUK MENINGKATKAN INTOLERANSI AKTIVITAS DI RUANG HEMODIALISA RSUD KABUPATEN REJANG LEBONG TAHUN 2025

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INTRADIALYTIC EXERCISE, COGNITIVE BEHAVIORAL THERAPY, AND DEEP BREATH RELAXATION FOR QOL IN HEMODIALYSIS PATIENTS: SYSTEMATIC REVIEW

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ABSTRACT

Chronic kidney disease (CKD) patients undergoing continuous hemodialysis (HD) experience decreased daily physical activity, lower tolerance to exercise and poorer health-related quality of life. Thus, HD patients need interventions that focus on their physical and psychological characteristics to improve their quality of life. This study aims to discuss the effectiveness of intradialytic exercise, cognitive behavior therapy and deep breath relaxation in improving the quality of life of hemodialysis patients. The study used a systematic literature review design to identify articles on intradialytic exercise, cognitive behavior therapy and deep breath relaxation from 2019-2023 was obtained from PubMed, ScienceDirect and Google Scholar. Seven studies found that intradialytic exercise enhances CKD patients' quality of life during hemodialysis. Four studies noted cognitive behavioral therapy's positive impact on physiological aspects, enhancing patients' well-being. Additionally, six studies observed deep breath relaxation's beneficial effects on physiological parameters, ultimately enhancing patients' quality of life during hemodialysis. Intradialytic exercise, cognitive behavior therapy and deep breath relaxation are effective in improving the quality of life of hemodialysis patients. Furthermore, these three interventions helped accelerate the medical approach to chronic kidney disease.

Keywords:
Cognitive behavior therapy, Deep breath relaxation, Hemodialysis, Intradialytic exercise, Quality of life

BACKGROUND

Chronic Kidney Disease (CKD) is a disease with a poor prognosis that causes the loss of renal function and progresses to the end stages of renal disease (ESRD) (Evans et al., 2022). Approximately 5.1 million ESRF patients worldwide; rely on renal replacement therapy for better survival, that is either peritoneal dialysis, hemodialysis, or kidney transplantation, and this number is expected to double in the next decade (Hamed & Aziz, 2020). Hemodialysis (HD) is the most common invasive and complex form of renal replacement therapy (Canaud et al., 2020). Nevertheless, the rapid improvement in HD techniques has recently contributed to an increase in the survival of CKD patients, on the other hand resulting in a variety of physical and mental complications, which may contribute to a decline in patients' quality of life (QoL) (Kim et al., 2022).

QoL is identified as a vital health outcome for studies evaluating the quality of healthcare, assessing the influence of illness and analyses of cost-effectiveness (Khatib et al., 2018). Lower quality of life scores are associated with a significant risk of hospitalization and mortality (Ravera et al., 2021), because changing how individuals perceive and evaluate their lives and illnesses may lead them to not adhere to treatment (Hagemann et al., 2019). Since the patient is at high risk of fatality, QoL becomes an important component as it is a parameter of successful intervention.

Studies focusing on the QoL of patients with CKD were published in online databases. For example, intradialytic exercise (IDE) has demonstrated a positive effect on the overall health and hospitalization rate of HD patients (Albadr et al., 2020). IDE could benefit patients undergoing hemodialysis in improving most domains of generic HRQOL (Hu et al., 2022). IDE has shown to have positive effects in HD patients; this was evident from the results of previous studies where IDE improved the efficiency of dialysis (Kt/V) (Vogiatzaki et al., 2022; Malini et al., 2022), VO2 max (Amalia et al., 2022), and QoL (Sovatzidis et al., 2020).

Related to cognitive behavior therapy (CBT) in CKD, several studies were completed. Astuti & Utami (2021) used CBT for treating depression in chronic kidney disease patients and have shown that depression decreased in patients with CKD. CBT has shown an encouraging effect on depressive symptoms and mental summary of QoL among HD patients (Ling et al., 2020). CBT therapy is very effective as it produces positive outcomes to patients, improves QoL and coping skills, treats problematic behavior and improves the illness disorder (Greenberg et al., 2019).

In addition to these two therapies, several studies have been conducted regarding deep breath relaxation in CKD. Deep breathing relaxation can lower anxiety, sleep quality, and fatigue in HD patients (Krismiadi et al., 2023). Deep breathing relaxation could become beneficial in reducing fatigue associated with HD (Eroglu & Metin, 2022). Deep breathing, according to other studies, maintains a balance between the sympathetic and vagal systems and, as a result, improves heart rate (Jensen et al., 2022). Deep breathing also helps individuals with advanced heart illness, as well as improving fatigue, sleep, and overall QoL (Rashid et al., 2023).

The evaluation results of existing studies used IDE, CBT and deep breathing relaxation as separate treatments in patients with CKD. However, the combination of these treatments was not addressed in any of the studies. Many studies did not combine treatment with CBT or deep breathing relaxation; they used IDE only. In fact, the combination accelerates the alleviation of clinical symptoms caused by dialysis. By controlling negative thoughts and reducing hopelessness and anxiety, it also improves QoL. Therefore, this study aims to evaluate the effectiveness of intradialytic exercise, cognitive behavior therapy, and deep breath relaxation in improving the QoL of HD patients in hospital. The findings of this study are expected to help nurses in managing HD patients' health conditions related to QoL.

METHODS

Research design: The study used a systematic literature review design to identify articles on intradialytic exercise, cognitive behavior therapy and deep breath relaxation in HD patients. This systematic review and meta-analysis followed the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines. The search involves online databases including PubMed, ScienceDirect and Google Scholar.

Search methods: The search criteria were studies on IDE, CBT and deep breath relaxation on HD, written in English, review studies are the primary source, whole research design and 2019-2023 publications. Keywords were as follows: 'intradialytic exercise,' 'CBT for hemodialysis,' 'deep breath relaxation for hemodialysis,' 'intradialytic exercise for hemodialysis,' 'CBT for HD,' 'deep breath relaxation for HD,' 'Quality of life intradialytic exercise HD,

'intradialytic, CBT and deep breath relaxation for HD patients' quality of life'.

Inclusion and exclusion criteria: The eligibility criteria for this systematic review were experimental studies, studies on IDE, CBT and deep breath relaxation interventions on HD, and study sites in any country. Exclusion criteria for this systematic review included studies whose participants were other than experimental studies and whose participants were not renal failure patients. Improved quality of life was the outcome assessed in this systematic review.

Data extraction: This systematic review examined the effectiveness of IDE, CBT and deep breath relaxation interventions in improving the quality of life of hemodialysis patients in hospitals. Therefore, the data extracted for this systematic review included study location, participant characteristics, intervention description, duration, outcome instruments, and safety protocols.

Quality appraisal: The study used a PRISMA protocol (Park et al., 2022). The authors also assessed the risk of bias in each study using The Joanna Briggs Institute (JBI) Critical Appraisal tool for use in JBI Systematic Reviews (Munn et al., 2023).

Data analysis: The methodology employed for data analysis within this study entails the utilization of narrative synthesis, a comprehensive approach aimed at elaborating and amalgamating research findings through qualitative summarization and synthesis.

RESULTS

Search Result

Based on the results of a literature search through publications in three databases: researchers found 509 articles that matched these keywords. The search results were then checked for duplication, and inclusion and exclusion were carried out according to the criteria while assessing the feasibility of the studies. Ultimately, 17 articles were obtained, which deserved discussion in this study (Figure 1). Fourth, 17 papers comparing and contrasting intradialytic exercise and CBT were considered (Table 1).

Characteristics of The Selected Studies

Seventeen studies were found, with seven focusing on the effectiveness of intradialytic exercise in enhancing the quality of life (QoL) for CKD patients undergoing HD. Additionally, four studies investigated how cognitive behavioral therapy benefits the physiological aspects of HD patients, consequently improving their QoL. Furthermore, six studies explored the positive impact of deep breath relaxation techniques on the physiological well-being of HD patients, leading to enhancements in their QoL.

Characteristics of The Selected Studies

Overall, the articles obtained examined patients with HD using various research methods, namely 10 studies using randomized controlled trials, 6 studies using quasi-experimental studies, and 1 study using single-blind clinical trials. There were 11 studies that used comparison therapy and 6 studies that did not use it.

The countries studied are Taiwan (Chang et al., 2022; Moeinzadeh et al., 2022), Indonesia (Suhardjono et al., 2019; Rochmawati et al., 2022; Krismiadi et al., 2023; Sutinah & Azhari, 2020; Sari et al., 2023), Brazil (do Valle et al., 2020), India (Valsaraj et al., 2021; Grover et al., 2022; Kharbteng et al., 2020), Korea (Kim et al., 2022), USA (Shirazian et al., 2023), China (Liao et al., 2020), Iran (Zhianfar et al., 2020; Aliakbari et al., 2021), Egypt (Hamed & Aziz, 2020).

DISCUSSION

The level of daily physical activity and physical performance in HD patients is much less than in healthy individuals, especially on dialysis days, and this sedentary lifestyle is associated with higher morbidity and mortality and they are less driven towards exercises (Moeinzadeh et al., 2022; Grover et al., 2022; do Valle et al., 2020). Physical activity results in better pulmonary, physical function, and well-being. The within group (pre- to post-intervention) comparison of VO2 max, QoL, sleep questionnaire, and rate of perceived exertion showed significant difference (Grover et al., 2022). Chang et al. (2022) reported that there is emerging evidence in support of intradialytic exercise improving health-related quality of life for patients on HD. Kidney Disease and Quality of Life (KDQOL) and recovery time could improve in HD patients after 12 week intradialytic cycling exercise (Moeinzadeh et al., 2022). Suhardjono et al. (2019) also found that patients who performed the twice-a-week intradialytic aerobic or combination physical exercise programs for 12 weeks exhibited significantly improved strength of their lower extremities and physical components of the dialysis QoL index. Intradialytic exercise is effective in increasing frailty, the value of dialysis adequacy in terms of Kt/V, urea retention rate values, reducing blood pressure, physical capacity, maximal oxygen consumption, sleep quality and improving QoL and fatigue

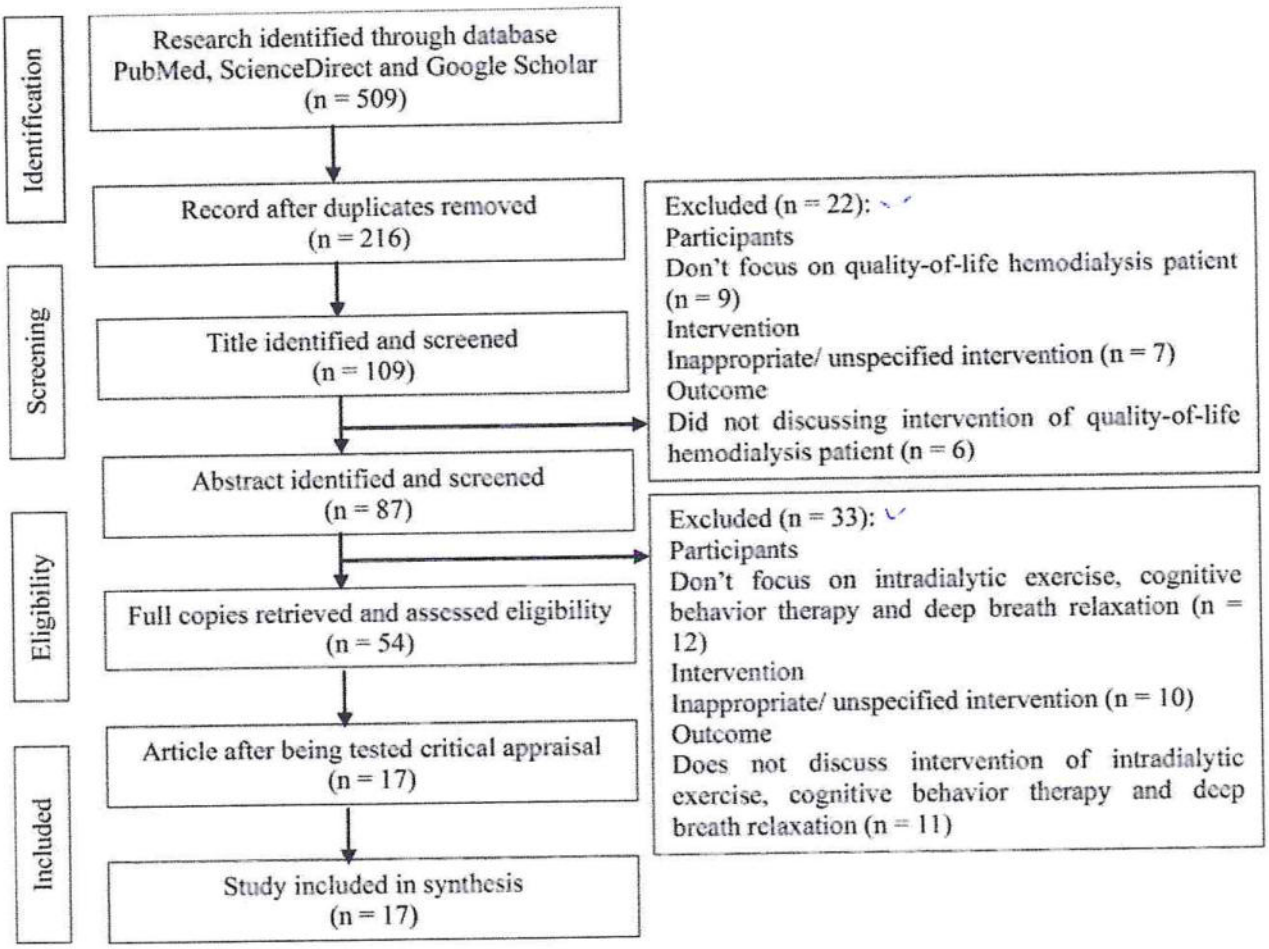

Figure 1. Article Selecting Process Used a PRISMA protocol

(Rochmawati et al., 2022; do Valle et al., 2020; Grover et al., 2022; Kim et al., 2022).

While HD techniques contribute to improved survival of CKD patients, they also result in various physical and mental/psychological complications, which may contribute to a decrease in patients' QoL (Gültekin et al., 2022). To improve the treatment effect of hemodialysis patients, in addition to IDE, many intervention regimens have also been used for hemodialysis patients, such as education, psychology, and continuing care. The assessment contents include negative emotions, QoL and some other clinical indicators (Liao et al., 2020). Cognitive behavioral intervention is a widely used psychotherapy among psychological care interventions. It can effectively alleviate anxiety and depression of HD patients and improve their QoL and renal function (Liao et al., 2020). And a simple CB-based behavioral-education can improve QoL and self-care in patients on HD (Shirazian et al., 2023). Moreover, CBT may potentially safeguard the cognitive functions of patients from degeneration. Empirical evidence suggests that CBT is effective in mitigating cognitive impairments (Zhianfar et al., 2020). Integrating CBT with renal replacement therapy, such as HD, appears to be a logical approach to enhance the overall welfare of the patient (Valsaraj et al., 2021). Additionally, the aforementioned four studies on the implementation of CBT demonstrate a rise in QoL and a reduction in depression, both of which are indicative of QoL (Zhianfar et al., 2020; Valsaraj et al., 2021).

Another promising intervention to improve the QoL of patients with HD is deep breath relaxation. Deep breathing exercises maximize the amount of oxygen supplied to the tissues resulting in production of more energy leading to reduction in levels of fatigue. Reduction in oxidative stress, increase of cellular energy and elasticity of blood vessels and improved circulation are the benefits of deep breathing relaxation techniques (P & Lobo, 2021). Deep breath relaxation can reduce anxiety, sleep quality, and fatigue because it uses spiritual values that can improve the QoL of HD patients (Krismiadi et al., 2023; Sutinah & Azhari, 2020; Sari et al., 2023). Hamed & Aziz (2020) also found that performing deep breathing exercises for twenty minutes, twice

Table 1. The Research Journal

No	Author and year of publication	Country	Research Design	Intervention	Comparison therapy (If any)	Outcome
1	Chang et al. (2022)	Taiwan	A randomized controlled trial	Intradialytic Exercise	Usual Care	Intradialytic exercise improves QOL
2	Moeinzadeh et al. (2022)	Taiwan	A randomized controlled trial	Intradialytic cycling exercise	Received no exercise plan	Intradialytic exercise improves QOL
3	Suhardjono et al. (2019)	Indonesia	A randomized controlled trial	Intradialytic exercise	No exercise	Intradialytic exercise improves PCS of QOL
4	Rochmawati et al. (2022)	Indonesia	Quasi-experimental design	Motion exercise	None	Positive effect on QOL
5	do Valle et al. (2020)	Brazil	A randomized controlled trial	Intradialytic resistance training	Lower limb stretching exercises	Positive effect on QOL
6	Grover et al. (2022)	India	Quasi-experimental design	Intradialytic exercises (IDE)	None	Positive effect on QOL
7	Kim et al. (2022)	Korea	A randomized controlled trial	Intradialytic aerobic exercise program	The education session	Intradialytic exercise improves PCS of QOL
8	Shirazian et al. (2023)	USA	A randomized controlled trial	Cognitive behavioral strategies	Daily care	CBT improves QOL
9	Liao et al. (2020)	China	A randomized controlled trial	Nursing intervention of cognitive behavioral therapy	Conventional care	CBT improves QOL
10	Zhianfar et al. (2020)	Iran	A randomized controlled trial	Multifaceted educational intervention of cognitive behavioral therapy	Daily care	CBT improves QOL
11	Valsaraj et al. (2021)	India	A randomized controlled trial	Cognitive behaviour therapy	Regular maintenance	CBT led to significant improvements in QOL
12	Krismiadi et al. (2023)	Indonesia	A quasi-experimental pre-post test	Benson relaxation technique and deep breath	Benson relaxation techniques	Deep breath relaxation improves QOL
13	Sutinah & Azhari (2020)	Indonesia	Quasi-experimental design	Relaxation breathing	None	Deep breath relaxation in reducing fatigue (parameter of QOL)

per day for a full month; can reduce maintenance HD patients' fatigue level. And research conducted by Kharbteng et al. (2020), which explains that breathing training programs carried out for four weeks

14	Sari et al. (2023)	Indonesia	Quasi-experimental design	AROM with deep breathing exercise	The hospital program	Deep breath relaxation improves QOL
15	Hamed & Aziz (2020)	Egypt	Randomized Quasi-experimental Study	Deep breathing exercise training	Routine care	Deep breath relaxation in reducing fatigue (parameter of QOL)
16	Aliakbari et al. (2021)	Iran	A single-blind clinical trial	Breathing exercise	None	Deep breath relaxation improves physical and mental health (parameter of QOL)
17	Kharbteng et al. (2020)	India	A randomized controlled trial	A breathing training program	None	Deep breath relaxation improves QOL

can improve the physical performance and QoL of HD patients.

The breathing training program will also stimulate impulses to the thalamus, which are then forwarded to the sensory processing area in the neocortex (frontal lobe) to increase a positive mood. Feelings of relaxation and calm will stimulate the limbic system to release neurotransmitters in the form of serotonin, dopamine, and melatonin, while the hypothalamus will release endorphins (Hamed & Aziz, 2020). Increased endorphins can affect the decrease in cortisol which has an impact on feeling relaxed, reducing tension, increasing feelings of pleasure, making a person more comfortable, and launching oxygen delivery to the muscles so that it can reduce levels of fatigue, anxiety, stress, and depression which will affect the QoL of patients (Neto et al., 2020; Al Naamani et al., 2021). And deep and silent breathing lowered respiratory rate and dyspnea enhanced VO2max. These exercises can be a useful tool for improving physical and mental health in these people, and they come at no cost to them. These breathing exercises are also simple to conduct because these patients are unable to participate in out-of-home sporting activities due to their physical limitations (Aliakbari et al., 2021).

The discussion underscores the profound impact of interventions like intradialytic exercise, cognitive behavioral therapy (CBT), and deep breath relaxation on enhancing the quality of life (QoL) for individuals undergoing hemodialysis (HD). Intradialytic exercise programs have demonstrated significant improvements in physical capacity, sleep quality, and overall QoL, while also mitigating frailty and reducing blood pressure. CBT interventions have proven effective in alleviating anxiety, depression, and enhancing cognitive functions, thereby contributing to improved QoL. Similarly, deep breath relaxation techniques have shown promise in reducing anxiety, fatigue, and enhancing sleep quality through the release of neurotransmitters and endorphins. These interventions offer accessible and feasible strategies to address both the physical and psychological aspects of HD patients' conditions, ultimately aiming to improve their overall well-being and treatment outcomes.

The study's strengths lie in its comprehensive review of interventions targeting the quality of life (QoL) in hemodialysis (HD) patients, encompassing intradialytic exercise, cognitive behavioral therapy (CBT), and deep breath relaxation. By drawing from multiple studies, it adopts an evidence-based approach, enhancing the reliability and validity of its conclusions. Additionally, the study offers practical implications by highlighting accessible strategies to address both the physical and psychological aspects of HD patients' conditions.

However, several limitations should be noted. Firstly, there's a lack of direct evidence on the combined effects of these interventions, necessitating further research to explore their synergistic impacts. Secondly, the heterogeneity among studies in methodology, patient populations, and outcome measures may limit the generalizability of findings. Despite these limitations, the study provides valuable insights into potential avenues for improving the QoL of HD patients through integrated interventions.

Thus, the need for research that combines intradialytic exercise, cognitive behavioral therapy (CBT), and deep breath relaxation has significant potential for enhancing the quality of life (QoL) in hemodialysis (HD) patients. Each intervention individually improves various aspects of QoL-physical capacity, mental well-being, and treatment satisfaction. Together, they address both physical and psychological dimensions simultaneously. Intradialytic

exercise improves physical capacity and sleep quality, while CBT alleviates anxiety, depression, and enhances cognitive functions. Deep breath relaxation reduces anxiety, fatigue, and enhances sleep quality. However, implementing combined therapies requires careful planning and coordination among healthcare professionals, tailored to individual patient needs. Further research, including randomized controlled trials, is needed to evaluate their long-term efficacy and benefits for HD patients.

CONCLUSION

Intradialytic exercise, cognitive behavior therapy and deep breath relaxation are effective in improving the quality of life of hemodialysis patients. Furthermore, these three interventions helped accelerate the medical approach to chronic kidney disease.

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Effects of Intradialytic Exercise on Dialytic Parameters, Health-Related Quality of Life, and Depression Status in Hemodialysis Patients: A Randomized Controlled Trial

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Abstract: Exercise is fundamentally important in managing chronic diseases and improving health-related quality of life (HRQL). However, whether intradialytic exercise is safe through assessment of changes in dialytic parameters and has a positive impact on HRQL and depression status of hemodialysis patients requires further research with diverse racial and cultural populations to identify. This study aimed to evaluate the effects of intradialytic exercise on dialytic parameters, HRQL, and depression status in hemodialysis patients. A randomized controlled trial was conducted at a medical center in Northern Taiwan. Sixty-four hemodialysis patients were recruited using stratified random sampling. Participants were randomized into an experimental group (EG, $n = 32$) or a control group (CG, $n = 32$). The EG received a 12-week intradialytic exercise program while the CG maintained their usual lifestyles. Dialytic parameters, HRQL, and depression status were collected at baseline and at 12 weeks. The results indicated no differences in the dialytic parameters from the baseline between both groups. However, the EG had increased HRQL ($ß = 22.6$, $p < 0.001$) and reduced depression status ($ß = -7.5$, $p = 0.02$) at 12 weeks compared to the CG. Therefore, a 12-week intradialytic exercise regime is safe and effective in improving HRQL and reducing depression status for hemodialysis patients.

Keywords: depression status; exercise; hemodialysis; intradialytic exercise; health-related quality of life

1. Introduction

End-stage renal disease (ESRD), the last stage of chronic kidney disease due to its irreversible loss of renal function, is an emerging global public health problem [1,2]. Nearly 90% of ESRD patients require regular hemodialysis as renal replacement therapy for maintaining survives [1]. However, ESRD patients on hemodialysis maintenance with associated multi-comorbidities (i.e., cardiovascular disease, renal bone disease, and anemia), experience an impaired health-related quality of life (HRQL) [2,3], and increased depression status due to the high burden of somatic symptoms and psychological distress [2,4,5]. In addition, both HRQL and depression status has been reported to be associated with

mortality in hemodialysis patients after adjusting for age, gender, race, the primary cause of kidney failure, dialysis vintage, and baseline depression history [4,5]. Therefore, developing strategies to improve HRQL and reduce depression status in hemodialysis patients is an imperative issue.

Physical inactivity, a prominent contributor to the deterioration of physical function among hemodialysis patients [6], has been linked to adverse clinical outcomes such as high morbidity rate and mortality [3,7]. Impairments from complications including fluid retention, anemia, and accumulated uremic toxins are attributable to the disease of ESRD itself, hemodialysis (e.g., the long periods of immobility during treatments and post-dialysis fatigue), and particularly, physical inactivity [6,7]. A vicious circle hence arises between physical inactivity and morbidity in hemodialysis patients.

A systematic review advocated that reduction in physical function of hemodialysis patients can be partially reversed with regular exercise over at least eight weeks [8,9]. In addition, engagement in regular exercise is associated with a decreased mortality risk [3,10], improved HRQL, and reduced depression status among hemodialysis patients [8,11]. Therefore, the National Kidney Foundation and clinical practice guidelines recommend that hemodialysis patients should increase their physical activity levels and make regular exercise a part of the strategic management of hemodialysis treatment [12]. Unfortunately, most hemodialysis patients exhibit low physical activity levels [13,14] for various reasons. Numerous known barriers, involving fear of injuries, discomfort, safety concerns, limited leisure time, symptoms of debilitation, and intolerance of exercise, make most hemodialysis patients experience difficultly in participating in regular exercise [15–17]. The most commonly reported barriers are fatigue on dialysis days and shortness of breath on non-dialysis days [15]. In addition, fatigue and muscle weakness after a long period of hemodialysis results in deconditioning, which might further reduce exercise tolerance, compliance/adherence to exercise, and overall motivation [18].

Despite regularly implemented supervised exercise interventions may not be entirely feasible for most chronic diseases in clinical practice, it has been reported to be more effective than home-based or community-based exercise training [19,20]. Hemodialysis patients must receive dialysis treatments regularly two to three times per week at a hospital or dialysis facility to maintain their lives. Therefore, adding exercise to a regular hemodialysis visit would be feasible and an optimal choice for hemodialysis patients under the assumption that it would increase exercise adherence. However, hemodialysis patients experience high cardiovascular and all-cause mortality, particularly during hemodialysis treatments. According to reports from the US Renal Data System database, two-thirds of cardiac deaths are attributed to an arrhythmia-related sudden death, making up 26% of mortality among hemodialysis patients [21]. Although many triggers of sudden death have been identified, such as acute myocardial ischemia, autonomic imbalance, increased sympathetic activity, history of hypertension, and diabetes, the higher risk of sudden death among hemodialysis patients appears to accelerate after dialysis initiation [21,22]. Therefore, whether a moderate-intensity intradialytic exercise intervention is safe requires further investigation, particularly through evidence with diverse racial and cultural groups. The clinical signs and characteristics (i.e., electrolyte imbalances, anemia, and hyperparathyroidism) frequently presented in hemodialysis patients could explain partial mechanisms of arrhythmia, as suggested by the relationship between sudden cardiac death and hemodialysis [23]. In addition, a decreased glomerular filtration rate (GFR) has been proposed to cause endocardial as well as diffuse myocardial fibrosis that could enhance the risk of life-threatening ventricular arrhythmias [24]. Hence, our study aimed to confirm the safety of a 12-week intradialytic exercise program by investigating the changes of serum chemistries, serum electrolytes, and GFR from baseline.

So far, whether intradialytic exercise is safe requires more research with diverse racial and cultural populations to identify, since previous reports evaluated the adverse or accident events during exercise training to determine the safety and particularly limited evidence were found in the Asian population [25]. In addition, inconsistent effects of

intradialytic exercise on HRQL are found [26–28] and little is known about the effects of a 12-week intradialytic exercise regime on cardiometabolic factors combined with HRQL and depression status. Therefore, the current study aimed to determine the effects of a 12-week intradialytic exercise program on dialytic parameters, cardiometabolic factors, HRQL, and depression status in hemodialysis patients.

2. Materials and Methods

2.1. Design

A randomized controlled trial with a two parallel-group design was conducted. Eligible ESRD patients undergoing maintenance hemodialysis for at least six months were randomized into either an experimental group (EG) or a control group (CG). The EG received a 12-week intradialytic cycling exercise and the CG maintained their usual lifestyles. Outcome measures including dialytic parameters (i.e., serum chemistries, serum electrolytes, intact-parathyroid hormone [IPTH], and estimated glomerular filtration rate [eGFR]), cardiometabolic factors (i.e., resting heart rate, systolic/diastolic blood pressure, fasting blood glucose, cholesterol, and triglycerides), and Uric acid), HRQL, and depression status were collected at pre- (baseline) and post- (12 weeks) intervention.

2.2. Participants

Potential hemodialysis patients were recruited from the hemodialysis center at a medical center in Northern Taiwan between June 2019 and December 2019. One hundred sixty-three patients receiving regular hemodialysis (97 patients treated on odd weekdays [Monday, Wednesday, Friday] and 66 patients treated on even weekdays [Tuesday, Thursday, Saturday]) were initially approached. Those who agreed to participate were then screened for eligibility by a nephrologist. Inclusion criteria were: (1) ESRD patients on hemodialysis maintenance; (2) aged 20 to 80 years; (3) able to speak and understand Mandarin; (4) had received regular treatment with hemodialysis (3 times/week) for at least six months, and (5) agreed to be randomized into one of the two groups. Exclusion criteria included lower limb disabilities, hospitalized patients, treatment with peritoneal dialysis, received hemodialysis less than three times/week, a history of recent acute myocardial infarction, unstable angina, uncontrolled arrhythmia, acute stroke, a hospitalization experience within the past six months, diagnosed cancer, and a mental illness, especially depression.

G*Power (Germany, version 3.1.9) software was applied for sample size estimation [29]. Based on an analysis of variance (ANOVA)-repeat measures (within-between interactions), a statistical power of 0.8, an effect size of 0.25, a significant level of 0.05, and the number of measurements at 2, we calculated that 26 participants in each group would be required [30]. By taking into account a possible attrition rate of 15–20%, the target sample size was set at 30–32 per group.

2.3. Study Cohorts and Interventions

Considering that having two groups in the same area for dialysis treatment combined with intradialytic exercise may result in bias, we used stratified random sampling to place participants into either the EG and CG and separated them into different treatment schedules. Therefore, 64 patients were randomly selected from 112 eligible patients (60 were treated on odd weekdays and 52 were treated on even weekdays) and allocated them with a 1:1 randomization ratio into the EG (n = 32, treated on odd weekdays) and the CG (n = 32, treated on even weekdays) by the research project investigator. Randomization was performed using sealed opaque envelopes which were opened by a research nurse.

The exercise protocol for the EG was prescribed by a rehabilitation physician and followed the principle based on the American College of Sports Medicine guidelines including frequency, intensity, time, and type [31]. (1) Frequency: received intradialytic, lower-limb, cycling exercise three times per week on alternative days (Monday, Wednesday, Friday) for 12 weeks (36 times) at the hemodialysis center of the medical center and supervised by hemodialysis nurses and a research nurse who had more than 10 years

of exercise training experience. (2) Intensity: the intensity of exercise was set at 12–14 (moderate-intensity: somewhat hard or reports of feeling a little bit tired but still ok to continue) based on the Borg's Perceived Exertion Rating Scale (a rating of 6 perceiving "no exertion at all" to 20 perceiving a "maximal exertion" of effort) [32]. Appropriate speed and grade of resistance were adjusted to achieve the required intensity. (3) Time: the duration of each exercise session consisted of a 5-min warm-up, 20-min endurance, and 5-min cool-down phase. The exercise occurred at least one to two hours after a meal. (4) Type: lower-limb ergometer (WP-698, Magnetic Mini Bike, Taiwan) was used for intradialytic cycling exercise in the supine position. Each session of intradialytic exercise started at 30 min after the beginning of hemodialysis when the hemodynamic stability of patients was confirmed (without complaint of chest pain, dyspnea, pallor, diaphoresis, or dizziness; had systolic pressure >200 mmHg or diastolic pressure >120 mmHg; had a decrease in systolic pressure of >10 mmHg compared to the systolic pressure at rest, or requested stopping the exercise). Participants in the CG maintained their usual lifestyles and regular hemodialysis.

2.4. Measures

Eligible patients who agreed to participate were invited to the local medical center for pre- (baseline) assessment. Data were collected using structured interviews with questionnaires (sociodemographics, lifestyle factors, HRQL, and depression status), blood analyses, and blood pressure measures at baseline and 12 weeks by a separate research nurse, blinded to the group assignment.

2.5. Dialytic Parameters

The trial assessed the safety of a 12-week intradialytic exercise program as compared with conventional treatment in hemodialysis patients through the stability or changes of dialytic parameters at pre- and post-intervention. We evaluated whether dialytic parameters including serum chemistries (red blood cell [count/uL], hemoglobin [g/dL], hematocrit [%], mean corpuscular volume [fL], albumin [g/dL], GPT [IU/L], GOT [IU/L], blood urea nitrogen [BUN, mg/dL], creatinine [Cr, mg/dL]), serum electrolytes (sodium [Na, mEq/L], potassium [K, mEq/L], calcium [Ca, mg/dL], phosphate [P, mg/dL]), IPTH [pg/mL]), and eGFR, [mL/min1.73m^2]) in the EG were different from the CG. All of the dialytic parameters were analyzed at the clinical laboratory of the local medical center, where was certified by the College of American Pathologists. The eGFR, calculated by the equation: 186 × (Creatinine/88.4) − 1.154 × (age) − 0.203 × (0.742 if female) × (1.210 if black), has been recognized as an indicator for facilitating the detection, evaluation, and management of chronic kidney disease [33].

2.6. Cardiometabolic Factors

The positive impact of regular moderate- to vigorous-intensity aerobic exercise on cardiometabolic health has been well-documented [34,35]. Therefore, the cardiometabolic factors, consisting of resting heart rate (beat/min), blood pressure (systolic and diastolic blood pressure [mmHg]), fasting blood glucose (mg/dL), serum lipids (cholesterol [mg/dL] and triglyceride [mg/dL]), and uric acid (mg/dL) were assessed at baseline and 12 weeks, as secondary outcomes. Resting heart rate and blood pressure were obtained after participants had been seated quietly for three to five minutes, using an electronic blood pressure monitor device (Terumo, ESP2000, Tokyo, Japan).

2.7. Health-Related Quality of Life

The well-valid and reliable Medical Outcomes Study Short-Form 36 (SF-36), consisting of 36 items and eight subscales (bodily pain [2 items], general health [5 items], mental health [5 items], physical function [10 items], role function limitation due to emotional problems [role-emotional, 3 items], role function limitation due to physical conditions [role-physical, 4 items], social function [2 items], and vitality [4 items]) except one item for health transition was used to assess HRQL [36]. In addition to the eight subscales, the total

mean score of HRQL was measured to evaluate the overall HRQL. Higher scores ranged from 0 to 100 presented better HRQL. Cronbach's alpha of the total scale in the present study was 0 93.

2.8. Depression Status

The 21-item, self-rated Beck Depression Inventory (BDI) [37] with good reported validity and reliability [38] was applied to measure participants' depression status. Scores ranged from 0–63 and higher scores indicated higher depression status. The BDI, comprising of emotional (5 items), cognitive (7 items), and somatic (9 items) categories, can also be used to screen depressive symptoms as minimal depression (0–9), mild depression (10–18), moderate depression (19–29), and severe depression (30–63). Cronbach's alpha of the scale in the present study was 0.92.

2.9. Ethical Consideration

Institutional review board approval (TSGHIRB: 1-108-05-070) was obtained from Tri-Service General Hospital in Taipei, Taiwan. This trial has been registered on the "ClinicalTrials.gov" (NCT04990154). All participants were invited to join the study after giving informed consent and were assured that their participation was entirely voluntary and that they could withdraw at any time.

2.10. Data Analysis

Statistical analyses were performed by SPSS version 16.0 (SPSS Inc., Chicago, IL, USA). Descriptive statistics including means, standard deviation (SD), and percentages (%) were used to display the study participants' sociodemographics, clinical information, and lifestyle characteristics. Student's t-tests and chi-square tests were used to compare the pre- and post-intervention differences between groups. Paired *t*-tests were applied to compare differences between pre- and post-tests. Generalized estimating equations (GEEs) for longitudinal data/repeat measures were applied to appraise the intervention effects of the two groups by significant interactions of group and time (group × time) as it can be used to evaluate intervention effects under adjustment for potential confounding factors [39]. Both the quantile-quantile plot and Shapiro–Wilk test were used to determine the normality of outcome variables studied. In addition, G*Power (Germany, version 3.1.9) software were also applied for the calculation of the post-hoc effect size under the sample size of 64 and resulted in an effect size of 0.35 [25]. An intent-to-treat analysis was applied to provide unbiased comparisons among the treatment groups and avoid the effects of patient dropouts. The last-observation-carried -forward method of data imputation was adopted to handle missing data. All of the statistical analyses were two-tailed and $p < 0.05$ was considered statistically significant.

3. Results

3.1. Baseline Characteristics of Participants

One hundred sixty-three patients were initially approached. Of these, 15 participants declined to participate (due to anticipated discomfort and fatigue from intradialytic exercise) and 36 were excluded. Of the remaining 112 participants, 64 were randomly selected and assigned: 32 (50%) to the EG (treated on odd weekdays) and 32 (50%) to the CG (treated on even weekdays). Of the 64 randomized participants, 57 (89%) completed all data collection (29 in the EG and 28 in the CG). The reasons for not completing the study were withdrawal from the study due to fatigue during intradialytic exercise ($n = 1$), suffering from knee osteoarthritis with severe pain ($n = 1$), and loss to follow-up due to hospitalization for coronary artery disease ($n = 4$) and pneumonia ($n = 1$) (Figure 1). The last-observation-carried-forward method of data imputation was used for intent-to-treat analysis. Hence, sixty-four participants were included in the data analysis.

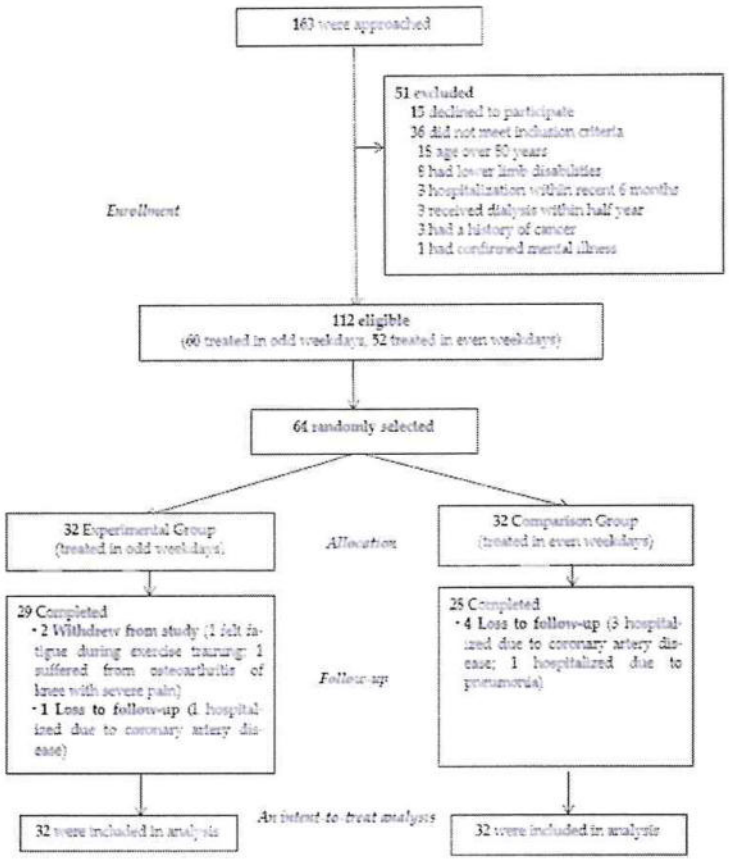

Figure 1. CONSORT Diagram of Participants' Flow Through the Trial.

Table 1 shows the sociodemographic characteristics, comorbidities, and lifestyle factors. The two groups did not differ in sociodemographics, comorbidities, and lifestyle factors. The baseline dialytic parameters, cardiometabolic factors, HRQL, and depression status in the two groups are shown in Table 2.

Table 1. Comparisons of demographics and comorbidity characteristics between groups.

Variables	EG $n = 32$	CG $n = 32$	t/x^2	p
Sociodemographic Characteristics				
Age (year), *mean (SD)*	62.0 (9.5)	62.1 (12.3)	0.03	0.97
Gender (male), *n (%)*	22 (68.8)	19 (59.4)	0.61	0.60
Marital status (married), *n (%)*	28 (87.5)	23 (71.9)	2.41	0.12
Education (more than high school), *n (%)*	21 (65.6)	25 (78.1)	1.24	0.27
Currently employed, *n (%)*	10 (31.2)	7 (21.9)	0.72	0.40
Body mass index (Kg/m^2), *mean (SD)*	23.4 (3.7)	23.4 (4.5)	−0.06	0.95
Duration of hemodialysis (year), *mean (SD)*	6.7 (5.7)	6.2 (5.1)	0.39	0.70
Comorbidities				
Hypertension, *n (%)*	28 (87.5)	24 (75.0)	1.64	0.34
Type 2 diabetes, *n (%)*	14 (43.8)	19 (59.4)	1.56	0.21
Hyperlipidemia, *n (%)*	5 (15.6)	6 (18.8)	0.11	0.74
Cardiovascular disease, *n (%)*	4 (12.5)	11 (34.4)	4.27	0.08
Metabolic syndrome, *n (%)*	6 (18.8)	7 (21.9)	0.10	0.76
Lifestyle Factors				
Smoking, *n (%)*	3 (9.4)	0 (0)	3.15	0.24
Drinking, *n (%)*	0 (0)	1 (3.1)	1.02	1.00

Note: *n*, number; SD, standard deviation; EG, experimental group; CG, comparison group.

3.2. Outcome Evaluation

3.2.1. Dialytic Parameters

The descriptive and univariate analyses of the outcome evaluation are shown in Table 2. There were no differences between the two groups in all of the baseline dialytic parameters. Given that participants in the EG had higher ($t = 2.43$, $p = 0.02$) albumin levels than those in the CG at 12 weeks, both EG and CG had no significant change in all of the dialytic parameters after 12 weeks. When the group × time interaction was examined based on the GEE analyses (Table 3), all of the dialytic parameters in the EG had no changes as compared to the CG.

3.2.2. Cardiometabolic Factor

There were no differences between the two groups in all of the baseline cardiometabolic factors (Table 2). Given that the EG had reduced systolic blood pressure ($t = -3.03$, $p = 0.004$) at 12 weeks as compared to the CG, both the EG and CG had no significant change in all of the cardiometabolic factors after 12 weeks. When the group × time interaction was examined based on the GEE analyses (Table 3), all of the cardiometabolic factors in the EG had no changes as compared to the CG.

3.2.3. Health-Related Quality of Life

There were no differences between the two groups in the baseline HRQL including the total mean score of HRQL and the eight subscales (Table 2). After the 12-week intradialytic exercise, the EG had an increased total mean score of HRQL, bodily pain, general health, mental health, physical function, role-physical, social functioning, and vitality. The CG had no changes within these from baseline. In addition, participants in the EG had a higher total mean score of HRQL and with most subscales except the bodily pain compared to the CG. When the group × time interaction was examined based on the GEE analyses, participants in the EG had a greater increase in total mean score of HRQL (ß = 22.6, $p < 0.001$), general health (ß = 19.2, $p = 0.004$), mental health (ß = 17.7, $p = 0.001$), physical function (ß = 14.5, $p = 0.02$), role-emotional (ß = 28.9, $p = 0.04$), and role-physical (ß = 63.7, $p < 0.001$) at 12 weeks as compared to those in the CG after adjusting for sociodemographic characteristics, comorbidities, and lifestyle factors (Table 3).

3.2.4. Depression Status

There were no differences between the two groups in baseline depression status (Table 2). After the 12-week intradialytic exercise, the EG had a significantly lower depression status while the CG rendered no changes. The significant group × time interaction for depression status revealed that the EG had a greater decrease in depression status at 12 weeks as compared to the CG (ß = −7.5, $p = 0.02$) after adjusting for sociodemographic characteristics, comorbidities, and lifestyle factors (Table 3).

Table 2. Differences of outcome indicators between groups at baseline and after the intervention.

Variables	EG (n = 32)			CG (n = 32)			Baseline		12-Week	
	Baseline	12-Week	p	Baseline	12-Week	p	EG vs. CG		EG vs. CG	
							t	p	t	p
Dialytic parameters										
Serum chemistries										
Red blood cell (×10^6/uL)	3.5 (0.6)	3.4 (0.6)	0.58	3.6 (0.7)	3.6 (0.9)	1.00	−0.46	0.647	−0.83	0.41
Hemoglobin (g/dL)	10.1 (1.4)	9.9 (1.1)	0.51	10.3 (1.3)	10.4 (1.3)	0.90	−0.676	0.50	−2.17	0.11
Hematocrit (%)	30.5 (4.2)	29.6 (3.6)	0.37	31.4 (4.4)	31.6 (5.6)	0.82	−0.827	0.411	−1.74	0.09
Mean corpuscular volume (fL)	87.9 (9.4)	88.1 (9.6)	0.95	89.0 (8.6)	93.1 (17.9)	0.31	−0.45	0.654	−1.35	0.18
Albumin (g/dL)	3.9 (0.3)	4.0 (0.3)	0.65	3.9 (0.3)	3.8 (0.2)	0.20	0.65	0.52	2.43	0.02
GPT (IU/L)	13.2 (4.2)	14.2 (4.5)	0.37	14.7 (7.1)	14.5 (7.4)	0.89	−1.05	0.30	−0.18	0.86
GOT (IU/L)	13.3 (4.9)	15.0 (6.8)	0.25	14.2 (6.1)	15.4 (6.6)	0.45	−0.68	0.50	−0.26	0.80
BUN (mg/dL)	65.6 (18.1)	70.4 (20.6)	0.33	65.8 (16.5)	70.5 (25.6)	0.39	−0.04	0.97	−0.02	0.99
Cr (mg/dL)	10.6 (2.2)	10.4 (2.3)	0.72	9.7 (2.0)	10.1 (2.1)	0.43	1.69	0.10	0.49	0.63
Serum electrolytes										
Na (mEq/L)	137.6 (3.0)	137.5 (2.4)	0.92	137.4 (2.8)	142.0 (24.5)	0.29	0.31	0.76	−1.04	0.30
K (mEq/L)	4.8 (0.8)	4.6 (0.6)	0.29	4.6 (0.7)	4.7 (1.1)	0.66	1.11	0.27	−0.40	0.69
Ca (mg/dL)	9.2 (1.2)	9.3 (1.1)	0.91	9.3 (1.0)	9.0 (0.9)	0.23	−0.13	0.90	1.16	0.25
P (mg/dL)	5.2 (1.4)	4.9 (1.2)	0.48	4.8 (1.2)	5.0 (1.3)	0.69	1.05	0.30	−0.06	0.95
IPTH (pg/mL)	416.3 (351.6)	438.7 (293.9)	0.79	330.9 (335.0)	321.8 (289.2)	0.93	0.81	0.42	1.47	0.15
eGFR (mL/min1.73m^2)	5.0 (1.1)	5.1 (1.2)	0.67	5.4 (1.5)	5.1 (1.3)	0.38	−1.415	0.162	−0.10	0.92
Cardiometabolic factors										
Systolic blood pressure (mmHg)	141.5 (20.8)	136.5 (14.4)	0.27	145.1 (8.0)	152.2 (25.5)	0.30	−0.58	0.562	−3.03	0.004
Diastolic blood pressure (mmHg)	75.6 (12.2)	71.7 (7.4)	0.13	73.1 (13.8)	74.8 (14.4)	0.62	0.76	0.451	−1.09	0.28
Resting heart rate (beat/min)	71.6 (8.3)	71.4 (8.5)	0.93	71.4 (9.8)	70.8 (9.7)	0.79	0.08	0.935	0.29	0.77
Fasting blood glucose (mg/dL)	105.4 (29.1)	103.6 (28.3)	0.81	125.8 (86.5)	116.8 (47.2)	0.61	−1.26	0.21	−1.36	0.18
Cholesterol (mg/dL)	156.6 (32.2)	153.8 (31.3)	0.73	156.5 (29.9)	157.4 (32.3)	0.92	0.01	0.99	−0.42	0.68
Triglyceride (mg/dL)	124.6 (127.6)	125.8 (116.2)	0.97	112.3 (62.9)	119.2 (86.5)	0.75	0.43	0.67	0.24	0.82
Uric acid (mg/dL)	6.4 (1.7)	5.7 (1.3)	0.16	6.2 (1.2)	6.0 (1.4)	0.64	0.60	0.55	−0.53	0.60
HRQL										
Total mean score	62.8 (17.5)	81.0 (18.7)	<0.001	64.1 (16.9)	58.1 (16.1)	0.15	0.30	0.77	5.27	<0.001
Bodily pain	74.4 (22.5)	90.8 (18.9)	0.003	79.9 (26.6)	79.9 (26.6)	1.00	0.89	0.38	1.89	0.06
General health	44.1 (17.6)	58.6 (20.6)	0.004	48.1 (18.8)	42.7 (19.8)	0.26	0.89	0.38	3.16	0.002
Mental health	63.8 (16.8)	79.8 (18.2)	0.001	70.6 (15.7)	67.4 (14.4)	0.39	1.69	0.10	3.02	0.004

Table 2. *Cont.*

Variables	EG (n = 32)			CG (n = 32)			Baseline		12-Week	
	Baseline	12-Week	p	Baseline	12-Week	p	EG vs. CG		EG vs. CG	
							t	p	t	p
Physical function	72.5 (21.0)	88.3 (15.7)	0.001	75.0 (19.3)	73.9 (19.1)	0.82	0.50	0.62	3.29	0.002
Role-emotional	78.1 (37.5)	90.6 (29.6)	0.14	63.5 (40.9)	44.8 (42.8)	0.08	−1.49	0.14	4.98	<0.001
Role-physical	46.9 (39.0)	85.9 (31.7)	<0.001	50.0 (43.1)	32.0 (39.3)	0.09	0.30	0.76	6.04	<0.001
Social functioning	71.9 (24.4)	88.7 (22.8)	0.01	72.3 (22.6)	70.7 (22.1)	0.78	0.07	0.95	3.20	0.002
Vitality	50.6 (20.6)	65.6 (21.1)	0.01	53.0 (19.1)	53.4 (18.1)	0.92	0.47	0.64	2.48	0.02
Depression status	12.8 (9.3)	5.0 (6.8)	<0.001	11.2 (9.8)	12.5 (9.2)	0.58	0.65	0.52	−3.73	<0.001

Note: EG, experimental group; CG, comparison group; GPT, glutamic pyruvic transaminase; GOT, glutamic oxaloacetic transaminase; BUN, blood urea nitrogen; Cr, creatinine; IPTH, intact parathyroid hormone; *eGFR*, estimated glomerular filtration rate; HRQL, health-related quality of life; data are presented as mean (SD); p-values were from the paired t-test, Student's t-test, or chi-square test.

Table 3. Evaluation of the intervention on dialytic parameters, health-related quality of life, and depression status based on the GEE Analysis.

Variables	Within Group		Between Group		Interaction Group (EG) × Time				Interaction [a] Group (EG) × Time			
	Ref: Baseline		Ref: CG		Reference Group: (CG) × Time				Reference Group: (CG) × Time			
	ß	p	ß	p	ß	95% C.I.		p	ß	95% C.I.		*p-Adjusted*
						Lower	Upper			Lower	Upper	
Dialytic parameters												
Serum chemistries												
Red blood cell (×10^6/uL)	0.001	1.00	−0.08	0.65	−0.08	−0.58	0.42	0.76	−0.03	−0.47	0.42	0.90
Hemoglobin (g/dL)	0.05	0.89	−0.22	0.51	−0.27	−1.13	0.59	0.54	−0.23	−1.03	0.58	0.58
Hematocrit (%)	0.29	0.82	−0.89	0.40	−1.17	−4.27	1.92	0.46	−0.96	−3.86	1.95	0.52
Mean corpuscular volume (fL)	4.07	0.28	−1.09	0.64	−3.90	−12.6	4.83	0.38	−3.82	−11.6	3.96	0.34
Albumin (g/dL)	−0.08	0.18	0.04	0.51	0.12	−0.07	0.30	0.21	0.11	−0.07	0.29	0.21
GPT (IU/L)	−0.25	0.89	−1.53	0.29	1.25	−2.85	5.35	0.55	1.42	−2.16	5.01	0.44
GOT (IU/L)	1.22	0.44	−0.94	0.49	0.50	−3.70	4.70	0.82	0.69	−3.26	4.63	0.73
BUN (mg/dL)	4.66	0.38	−0.19	0.97	0.09	−13.9	14.1	0.99	0.93	−12.2	14.1	0.89
Cr (mg/dL)	0.41	0.42	0.88	0.09	−0.61	−2.07	0.85	0.41	−0.53	−1.75	0.69	0.40

Table 3. *Cont.*

Variables	Within Group		Between Group		Interaction Group (EG) × Time				Interaction [a] Group (EG) × Time			
	Ref: Baseline		Ref: CG		Reference Group: (CG) × Time				Reference Group: (CG) × Time			
	ß	*p*	ß	*p*	ß	95% C.I.		*p*	ß	95% C.I.		*p-Adjusted*
						Lower	Upper			Lower	Upper	
Serum electrolytes												
Na (mEq/L)	4.68	0.28	0.22	0.76	−4.74	−13.3	3.77	0.28	−4.71	−12.8	3.34	0.25
K (mEq/L)	0.10	0.65	0.20	0.26	−0.29	−0.84	0.26	0.31	−0.27	−0.80	0.25	0.31
Ca (mg/dL)	−0.29	0.21	−0.03	0.90	0.33	−0.39	1.04	0.37	0.31	−0.38	1.00	0.38
P (mg/dL)	0.13	0.69	0.34	0.28	−0.36	−1.23	0.52	0.42	−0.30	−1.14	0.54	0.49
IPTH (pg/mL)	−9.09	0.93	85.38	0.40	31.49	−220.2	283.2	0.81	3.5	−227.5	234.5	0.98
eGFR (mL/min1.73m^2)	−0.31	0.37	−0.47	0.15	0.44	−0.44	1.32	0.33	0.40	−0.38	1.18	0.32
Cardiometabolic factors												
Systolic blood pressure (mmHg)	−7.06	0.28	−15.7	0.002	12.1	−3.44	27.6	0.13	−12.5	−26.5	1.37	0.08
Diastolic blood pressure (mmHg)	1.75	0.61	2.47	0.44	−5.59	−14.0	2.77	0.19	−5.80	−13.2	1.59	0.12
Resting heart rate (beat/min)	−0.66	0.79	0.19	0.93	0.47	−5.74	6.68	0.88	0.54	−5.29	6.37	0.86
Fasting blood glucose (mg/dL)	−8.94	0.60	−20.3	0.20	7.16	−29.2	43.5	0.70	5.80	−27.2	38.8	0.73
Cholesterol (mg/dL)	0.86	0.92	0.11	0.99	−3.67	−26.8	19.4	0.76	−8.69	−29.4	12.0	0.41
Triglyceride (mg/dL)	6.95	0.74	12.3	0.63	−5.72	−78.4	67.0	0.88	−4.18	−70.3	61.9	0.90
Uric acid (mg/d)	−0.22	0.64	0.22	0.25	−0.54	−1.83	0.75	0.41	−0.57	−1.78	0.65	0.36
HRQL												
Total mean score	−6.0	0.14	−1.3	0.76	24.2	12.4	36.0	<0.001	22.6	11.2	34.0	<0.001
Bodily pain	0.0	1.00	−5.5	0.37	16.4	0.1	32.7	0.05	12.8	−2.0	27.5	0.09
General health	−5.5	0.25	−4.1	0.36	20.0	6.9	33.1	0.003	19.2	6.3	32.1	0.004
Mental health	−3.3	0.38	−6.9	0.09	19.3	8.1	30.4	0.001	17.7	7.5	27.8	0.001
Physical function	−1.1	0.82	−2.5	0.61	16.9	4.0	29.7	0.01	14.5	2.1	27.0	0.02
Role-emotional	−18.8	0.07	14.6	0.13	31.3	5.3	57.2	0.02	28.9	2.1	55.8	0.04
Role-physical	−18.0	0.08	−3.1	0.76	57.0	30.8	83.3	<0.001	63.7	36.3	91.1	<0.001
Social functioning	−1.6	0.78	−0.4	0.95	18.4	2.7	34.0	0.02	13.9	−1.4	29.1	0.08
Vitality	0.5	0.92	−2.3	0.63	14.5	1.1	28.0	0.04	10.2	−3.4	23.7	0.14
Depression status	1.3	0.57	1.6	0.51	−9.1	−15.1	−3.1	0.003	−7.5	−13.8	−1.3	0.02

Note: EG, experimental group: exercise training; CG, control group: received routine usual care; ß: Regression coefficient; Analyses were performed by GEE models, with a Group × Time interaction term characterizing the intervention effect of interest; *p*-adjusted, [a] models were adjusted for sociodemographic characteristics (sex, age, educational level, marital status, current employment, body mass index, duration of hemodialysis), comorbidities (hypertension, type 2 disease, heart disease, hyperlipidemia, metabolic syndrome) and lifestyle factors (smoking and drinking).

4. Discussion

The results of the current study demonstrated that a 12-week intradialytic exercise intervention is effective in improving HRQL and decreasing depression status among hemodialysis patients, but presents no differences in the dialytic parameters, indicating the intradialytic exercise regime is safe for hemodialysis patients. Given that a 12-week, moderate-intensity intradialytic exercise program had no additional benefit in cardiometabolic factors, our study results add to the literature illustrating that intradialytic exercise has a positive impact on HRQL and depression status without remarkable adverse events in hemodialysis patients, highlighting its clinical benefit when it is provided in combination with hemodialysis treatments in ESRD patients.

During hemodialysis, large fluid volumes are extracted followed by delayed reuptake of water from the interstitial space which leads to an inability to normalize arterial plasma volume. This causes a decline in cardiac output and reduces myocardial and systemic perfusion in 20–30% of ESRD patients [40]. A recent review advocates the need for more research to assess the safety of intradialytic exercise for hemodialysis patients among diverse cultures or regions since most studies have been conducted with Western populations [25,26]. In addition, previous studies assessed the adverse or accident events during exercise training to determine the safety [25,26] instead of dialytic parameters such as serum chemistries, electrolytes, and GFR. The current study thus examined the effects of intradialytic exercise on the dialytic parameters, including serum chemistries (red blood cell, hemoglobin, hematocrit, mean corpuscular volume, albumin, GPT, GOT, BUN, Cr), serum electrolytes (sodium, potassium, calcium, phosphate), and IPTH in Asian population to determine its safety. Our findings showed that after a 12-week intradialytic exercise regime, the EG had no changes in all of the dialytic parameters as compared to the CG. This finding is consistent with previous research that has shown how intradialytic exercise had no significant effect on serum phosphate levels and PTH [25] as well as the serum calcium and hemoglobin levels [41]. In addition, some dialytic parameters such as hemoglobin and electrolytes might be influenced by an individual's nutritional status and dietary patterns. Future studies, therefore, must investigate these effects under standardized diet formulas in both groups.

A recent study also revealed how exercise benefits non-dialysis patients with chronic kidney disease by increasing eGFR [42]. However, there are scant references regarding its effects in hemodialysis patients or patients who participated in intradialytic exercise. In turn, this study evaluated the effects of intradialytic exercise on glomerular filtration rate, revealing that the EG had no changes in eGFR compared to the CG. The renal functions of the participated hemodialysis patients who reported an average hemodialysis duration of 6.2–6.7 years in this study indicate an irreversible progression, contributing to such an unchangeable result of the glomerular filtration rate. However, during exercise, the distribution of cardiac output shifting to the skeletal muscles would cause a decrease in renal blood perfusion. Additionally, the higher intensity of the exercise, the lower the proportionate distribution of cardiac output is found [42]. Whether receiving hemodialysis combined with intradialytic exercise may aggravate the reduction of renal perfusion during the training process remains for further research to identify. Our current study evaluated the effects of intradialytic exercise on the changes of glomerular filtration rate among hemodialysis patients, confirming the safety of a 12-week, moderate intradialytic exercise for hemodialysis patients. These findings are in line with previous reports [27,43]. In addition, during the 12-week intradialytic exercise, no adverse events, including intradialytic hypotension, were observed in our study except for two patients reporting exercise-related limb pain, which was consistent with previous reports [26,27]. We conjecture that acute physiological responses to intradialytic exercise may help increase blood volume by inducing greater reuptake of blood from tissue, contributing to hemodynamic stability [44]. Sheng and his colleagues identified that intradialytic exercise can even improve *Kt/V*, proving the safety of the exercise regimen [43]. Therefore, the current study used different parameters to add literature confirming the safety of a 12-week moderate-intensity intradialytic exercise

program in hemodialysis patients with a preliminary result investigating the association between intradialytic exercise and eGFR, providing considerations for future research to design alternative or various intradialytic exercise prescriptions in hemodialysis patients.

Substantial evidence concluded that exercise significantly improved patients' cardiometabolic health [45,46]. However, the effects of intradialytic exercise on cardiometabolic health remain limited, particularly involving Asian populations. Hence, we examined the effects of a 12-week aerobic intradialytic exercise on cardiometabolic health of Taiwanese hemodialysis patients and revealed no additional benefits in cardiometabolic factors including systolic/diastolic blood pressure, resting heart rate, fasting blood glucose, or serum lipids (cholesterol, triglyceride, and uric acid), which are in line with a previous study [43]. The reasons explaining these insignificant effects can be complicated. A prolonged exercise program over at least six months tends to have a positive impact on cardiometabolic health for hemodialysis patients [43]. In addition, a moderate-to-vigorous exercise regime would be a major predictor to decreased insulin resistance and improved cardiometabolic status [47]. Given that the intensity of exercise was moderate in our study, a subjective rating of intensity through individuals' perceived exertion is not entirely objective and possibly led to overestimations of the intensity of the exercise. Future studies are thus recommended to apply objective instruments to accurately measure the intensity of exercise, providing exercise training with adequate intensity.

Several previous studies have concluded that combining aerobic and resistance exercise tends to have a positive impact on cardiometabolic factors since combined aerobic exercise and strength training reveals more favorable results regarding improved cardiorespiratory fitness [48]. Cardiorespiratory fitness is a component of physiological fitness that relates to the circulatory and respiratory system's ability to supply oxygen during sustained physical activity. However, several causes such as anemia, muscular atrophy, hypervolemia, cardiac dysfunction, and physical deconditioning lead hemodialysis patients to an extremely low level of cardiorespiratory fitness [48]. Participants in this study presented a relatively aging population, thus this problem may have been exaggerated.

Hemodialysis patients experience a heavy burden of symptoms and are more inactive, leading to poor functional capacity and a decreased HRQL [43,49], which our study confirms, particularly regarding a lower score of general health, role function limitation due to physical conditions (role-physical), and vitality. While a recent systematic review advocated that regular exercise may reduce depression and fatigue in hemodialysis patients [26], more randomized controlled trials that focus on different exercise regimens are required. Gomes and his research team examined the effects of different intradialytic exercise training modalities among hemodialysis patients and revealed that aerobic exercise alone was not significantly associated with physical function (i.e., aerobic capacity) and HRQL [28]. However, other research teams had different conclusions [25,27]. Given that substantial evidence examined the effects of intradialytic exercise on HRQL, inconsistent results were found, particularly result from different exercise modalities. To understand the effects of intradialytic exercise on HRQL in a specific exercise prescription is required and better to compare, identifying an optima exercise prescription for hemodialysis patients. Hence, our study examined the effects of a 12-week, moderate-intensity intradialytic exercise on HRQL and depression status in hemodialysis patients to provide further evidence for fulfilling the knowledge gap. Accordingly, we found an effectively positive impact on HRQL and depression status, involving the overall mean score, general health, mental health, physical function, and role function due to emotional problems (role-emotional), and role function due to physical conditions (role-physical), except for the subscales of bodily pain, social functioning, and vitality. In a previous systematic review, which is inconsistent with our study results, only the physical aspects of HRQL were improved rather than the mental aspects of HRQL after receiving intradialytic exercise [26]. Another review also suggested that aerobic exercise alone was not associated with HRQL improvement [28]. These differing results might attribute to a different follow-up period, exercise prescription (frequency, intensity, type, and time), or implementation of the exercise. In addition, possible rea-

sons for the changes in the mental domains of HRQL or psychological health (decreased depression) may be associated with factors contributing to patients' overall mental and emotional states such as disability, degree of dependence [50], the burden of the disease itself, financial problems resulting from unemployment, or available family/social support. Further research is therefore recommended to adjust for these potential confounding factors to accurately identify the mediators of HRQL and intradialytic exercise among hemodialysis patients.

Depression, which is associated with morbidity and mortality in hemodialysis patients [4,5,51], has been identified as the most prevalent psychological problem in hemodialysis patients. In the current study, we found that a 12-week intradialytic exercise is effective in decreasing depression status among hemodialysis patients. Whether this finding is attributed to frequent social interactions with medical staff during hemodialysis treatments, increased vitality, or increased confidence in the management of the disease is not known. Further efforts are required to illustrate this mechanism.

Intradialytic exercise for hemodialysis patients has emerged in recent studies. However, evidence remains insufficient and requires more high-quality clinical trials with diverse racial and cultural groups to clarify and reach conclusions. Therefore, we provided results pertaining to an Asian population to support this research gap. However, several limitations must be acknowledged in this study, including (1) a lack of long-term follow-up evaluation, (2) limited generalizability due to the sampling method (the EG and CG were only randomly selected from the treatment groups of specific days in the week) given that all of the sociodemographic factors, comorbidities, and lifestyle factors were similar between the groups, (3) a limited geographic region where the study was conducted, and (4) the use of a single urban medical center which limits its generalizability for rural areas. Hence, these findings must be interpreted with caution, and larger sample sizes, as well as more repeated evaluations with a longer follow-up period, are required. The strengths of this study include its random allocation design and the high rate of completion (89%) by the participants who were diagnosed with ESRD with a mean hemodialysis treatment period of 6.5 years. Therefore, since intradialytic exercise rendered better compliance/adherence among hemodialysis patients compared to protocols implemented outside hemodialysis centers [48], we recommend that intradialytic exercise combined with hemodialysis treatment should be integrated into clinical settings for hemodialysis patients.

5. Conclusions

A 12-week aerobic intradialytic exercise regime is safe and feasible for hemodialysis patients. Adding intradialytic exercise into the hemodialysis process has positive effects on improved health-related quality of life and decreased depression in hemodialysis patients. Further study designs are suggested to evaluate whether a longer duration, higher intensity, or different mode of exercise (such as a combination of aerobic exercise and strength/resistance training) benefits the dialytic parameters and cardiometabolic factors in hemodialysis.

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Informed Consent Statement: Written informed consent has been obtained from the patient(s) to publish this paper.

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Randomized Trial—PrEscription of intraDialytic exercise to improve quAlity of Life in Patients Receiving Hemodialysis

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Introduction: Whether clinically implementable exercise interventions in people receiving hemodialysis (HD) therapy improve health-related quality of life (HRQoL) remains unknown. The PrEscription of intraDialytic exercise to improve quAlity of Life (PEDAL) study evaluated the clinical benefit and cost-effectiveness of a 6-month intradialytic exercise program.

Methods: In a multicenter, single-blinded, randomized, controlled trial, people receiving HD were randomly assigned to (i) intradialytic exercise training (exercise intervention group [EX]) and (ii) usual care (control group [CON]). Primary outcome was change in Kidney Disease Quality of Life Short-Form Physical Component Summary (KDQOL-SF 1.3 PCS) from baseline to 6 months. Cost-effectiveness was determined using health economic analysis; physiological impairment was evaluated by peak oxygen uptake; and harms were recorded.

Results: We randomized 379 participants; 335 and 243 patients (EX $n = 127$; CON $n = 116$) completed baseline and 6-month assessments, respectively. Mean difference in change PCS from baseline to 6 months between EX and CON was 2.4 (95% confidence interval [CI]: −0.1 to 4.8) arbitrary units ($P = 0.055$); no improvements were observed in peak oxygen uptake or secondary outcome measures. Participants in the intervention group had poor compliance (47%) and poor adherence (18%) to the exercise prescription. Cost of delivering intervention ranged from US$598 to US$1092 per participant per year. The number of participants with harms was similar between EX ($n = 69$) and CON ($n = 56$). A primary limitation was the lack of an attention CON. Many patients also withdrew from the study or were too unwell to complete all physiological outcome assessments.

Conclusions: A 6-month intradialytic aerobic exercise program was not clinically beneficial in improving HRQoL as delivered to this cohort of deconditioned patients on HD.

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INTRODUCTION

Improved HD techniques and management of coexisting disease has improved the average life expectancy of patients receiving HD therapy globally, but disability and associated symptoms remain highly prevalent accounting for more life years lost to disability.[1] In the UK, 48% of the HD population report severe functional dependencies,[2] which impact on HRQoL.[3] Components of HRQoL, particularly the domain of physical functioning, stand out as the strongest predictor of survival, hospitalizations, and morbidity.[4] Knight *et al.*[5] and Lowrie *et al.*[6] report multiple symptoms that

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affect the physical component of HRQoL.[7] Moreover, higher levels of physical activity are associated with better scores in HRQoL measures, physical functioning, depression, and burden of kidney disease symptoms.[8]

The physical component of HRQoL, therefore, may be targeted with interventions to enhance physical activity. In patients receiving HD therapy, systematic reviews indicate that a range of exercise training interventions improve physical function and alleviate disability symptoms.[9–22] Of particular interest are studies investigating intradialytic exercise, as the environment of unit-based HD provides a platform for longer-term sustainable implementation of exercise rehabilitation programs.[23] The pre-existing need for patients to attend for standard thrice weekly, 4 hour-long HD sessions provides an opportunity to deliver a structured and supervised rehabilitation program with reduced patient burden regarding time, effort, and travel costs.[24,25] Thus, physical activity behaviors could be promoted using an implementation model that integrates physical activity into the main health care system for patients receiving HD therapy.

Nevertheless, very few dialysis units have chosen to implement this physical rehabilitation option in the UK. A barrier to implementation has been a lack of high-quality, adequately powered randomized controlled trials of intradialytic exercise with patient-reported outcomes (HRQoL), health economics (cost-effectiveness), and harms (serious adverse events [SAEs]) as the primary outcomes. Thus, the balance of benefits to costs and harms has been impossible to evaluate. Consequently, the PrEscription of intra-Dialytic exercise to improve quAlity of Life (PEDAL) trial was commissioned by the National Institute for Health Research to evaluate whether intradialytic exercise was able to improve HRQoL in patients receiving HD therapy. The primary objective was to determine, in stage 5 chronic kidney disease (CKD) patients receiving maintenance HD, whether usual care augmented by intradialytic exercise training for a period of 6 months improved KDQOL-SF 1.3 PCS.

METHODS

Trial Design and Oversight

We conducted this pragmatic prospective randomized controlled trial in 5 regions (London, Scotland, Wales, North-West England, and Midlands), across a total of 12 HD units, in the UK. The trial recruited prevalent patients with stage 5 dimensions of CKD receiving HD therapy. Briefly, the intervention consisted of using a modified cycle ergometer to perform aerobic exercise in a semirecumbent position, 3 times per week during the first 2 hours of HD. Twice per week, after the aerobic cycling exercise, participants completed lower extremity muscular conditioning exercises. These included 3 sets of 10 to 15 repetitions of dynamic resistance exercises for all major muscle groups. All exercises were performed against body weight before progression with ankle weights and TheraBands (Akron, OH). The exercise program was delivered and supervised by physiotherapy assistants.

London Fulham Research Ethics Committee approved the protocol (14/LO/1851), and all the participants provided written informed consent. The study was registered prospectively (ISRCTN N83508514). The trial protocol and details on inclusion/exclusion criteria, randomization procedure, and exercise intervention and prescription have been described elsewhere.[26] The Consolidated Standards of Reporting Trials Extension for Patient Report Outcomes also suggested reporting all the multi-item scales from the KDQOL-SF instrument.

Primary Outcome

The primary outcome for this study was the change in KDQOL-SF 1.3 PCS from baseline to 6 months.[27] The KDQOL-SF 1.3 instrument was chosen because of its validity in patients with CKD and inclusion of a generic core that has been widely used in CKD and other populations. The KDQOL-SF 1.3 is a disease-specific QoL measure that includes 43 kidney disease–targeted items and 36 items providing a generic core and an overall health-rating item. The questionnaire was completed by patients using pen and paper, with queries answered by research officers blinded to treatment allocation. Scoring followed currently recommended methods.[28] Thus, the PCS score can be interpreted as follows: a score above or below 50 is above or below the average, respectively, in the US general population, whereas a 1-point difference in the score is one-tenth of a SD. Analysis of within-trial change in the KDQOL-SF 1.3 PCS score from baseline, adjusted for baseline levels and randomization minimization variables, suggested that the study had 80% power to detect a 4-point difference with only 87 participants per group (with complete data at baseline and 6-month follow-up).

Secondary Outcomes

HRQoL, Cost-Effectiveness, and Harms

From the KDQOL-SF 1.3, the multi-item scale of energy/fatigue and the kidney disease–targeted items (burden of kidney disease) were presented as prespecified. In addition, the remaining 7 multi-item scales were presented. Then, a generic preference-based measure of HRQoL was obtained using the EuroQol 5-dimension descriptive system (EQ-5D-5L).[29] The EQ-5D-5L

comprises the following 5 dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. The EQ—visual analog scale was also obtained, whereby participants reported their self-rated evaluation of their health state on a 0 to 100 visual analog scale. Costs of delivering the PEDAL intervention were calculated, including exercise equipment, assumed to cost £1000 with a lifetime of 10 years and maintenance costs of £50 per year. Staff costs were assumed to include one ×0.6 full-time equivalent physiotherapy assistant (mid band 4 Agenda for Change scale, annual employer costs from £25,866 outside London to £34,787 in London) per 12 to 20 participants (to reflect different geographic spacing of kidney units in rural and urban areas) and one ×1.0 full-time equivalent supervisor (mid band 8 Agenda for Change, annual employer costs from £55,078.00 outside London to £71,418.96 in London) per 80 participants.

Physical Function

Upper limits of exercise tolerance were assessed by peak oxygen uptake determined by an incremental cycling protocol.[26] Physical function limitations were assessed by the sit-to-stand-60[30] and gait speed in 10 m.[31] Physical activity behaviors were captured by the International Physical Activity Questionnaire Short-Form[32]; ability to undertake activities of daily livings was recorded by the Duke Activity Status Index[33]; and fear of falling was assessed by the Tinetti Falls Efficacy Scale.[34]

Cardiovascular Risk and Clinical Measures

Arterial stiffness was assessed by the carotid–femoral pulse wave velocity,[35] measured using the Vicorder system (Skidmore Industries, UK) and by following the current recommendations.[35] Measures of body mass index and waist circumference were also recorded. Clinical data included cause of kidney disease, comorbidities, routine clinical blood tests (hemoglobin, serum phosphate, and parathyroid hormone), and medications (including erythropoiesis-stimulating agents).

Harms

Harms were actively recorded in both groups by the physiotherapy assistants from baseline to the end of the 6-month follow-up period ($n = 335$). Relationship to the intervention was evaluated by the lead clinician at each center, who was not blinded to treatment allocation. SAEs were reviewed by a data safety monitoring committee; rules for stopping the trial were that the committee identified a marked increase in expected or unexpected SAEs owing to the testing or intervention procedures. Data on hospitalizations and deaths (all-cause mortality and cardiovascular mortality) were collected by reviews of clinical databases and records at each study visit.

Compliance and Adherence (Fidelity) to Exercise Prescription

General compliance was recorded as the percentage of exercise sessions completed out of the total prescribed for the 6-month follow-up period. Adherence (fidelity) was recorded as the percentage of patients who adhered exactly to the prescribed exercise (cycling and muscle conditioning exercises) at the prescribed intensity and cycling time duration for each session across the 6 months. In addition, the percentage of patients who temporarily (>2 weeks) paused exercise was noted. These data were recorded by physiotherapy assistants through completion of sessional exercise diaries.

Statistical Analyses

The primary outcome measure (change from baseline to 6 months in KDQOL-SF 1.3 PCS) was compared between the control and intervention groups using a normal linear model adjusting for baseline KDQOL-SF 1.3 PCS and the randomization minimization variables (age, gender, diabetes status). The findings are presented as the adjusted mean difference (95% CI) between the treatment groups. Significance was set at $P \leq 0.05$. The main analysis was carried out on research participants with PCS assessments at baseline and 6 months. A total of 2 sensitivity analyses were also carried out, first imputing a score of 0 for those who died before 6 months and second based on all participants with a baseline PCS using the method of multiple imputation. As results were consistent between methods, only the main analysis is reported herein.

Secondary continuous outcomes were analyzed as for the primary outcome. For health economic data, we estimated the mean between-group difference in costs of the intervention and the mean between-group difference in quality-adjusted life years accrued by participants during the study, estimated as the area under the health utility curve from study entry (i.e., randomized and attended baseline visit) to follow-up (6 months after). Costs in the CON were set to 0. Estimated between-group differences in cost and quality-adjusted life years were obtained by the method of recycled prediction in 5000 bootstrap samples. The distribution of these quantities was summarized and presented graphically in the incremental cost effectiveness plane. Time-to-event outcomes (cardiovascular and all-cause mortality) were calculated as time from randomization and were compared between treatment groups using Cox proportional hazard regression models. The results are reported as the adjusted hazard ratio for intervention versus control (95% CI). Data involving counts of events (hospitalizations) were compared between treatment groups using negative binomial regression

models adjusting for length of follow-up. The results are reported as adjusted rate ratio (95% CI). Harms (SAEs) were tabulated by system organ class and body system using the Medical Dictionary for Regulatory Activities Terminology.[36] Recurrent events were counted separately. Compliance and adherence data were tabulated and presented visually.

RESULTS

Patient flow, including recruitment to and retention in the trial, is detailed in Figure 1. A total of 2409 patients were screened for eligibility. Nevertheless, 410 were not eligible per inclusion criteria, 660 patients declined to participate, and 990 patients were not eligible to participate owing to competing trials in this same population within the UK. A total of 335 participants attended a baseline study visit, 175 patients who were randomized to EX and 160 participants to CON. The primary outcome was known for 243 participants (73%) who attended a baseline visit, 116 participants (66%) in the exercise group, and 127 participants (79%) in the usual care group. More patients withdrew from EX (40; 34.5%) than CON (15; 11.8%) owing to participant decision, physician recommendation because of medical concerns, and transplantation. Apart from an increased number of smokers in the group of patients who withdrew from EX, no obvious differences in characteristics of the withdrawn and not withdrawn groups were present (Table 1).

Effect of Intradialytic Exercise Training on HRQoL

For the primary outcome, the mean difference in the change in PCS from baseline to 6 months between EX and CON was 2.4 (95% CI: −0.1 to 4.8) arbitrary unit and was not statistically significant ($P = 0.055$). Similarly, other measures of HRQoL (energy/fatigue, burden of kidney disease, EQ-5D-5L, and EQ-5D visual analog scale: Table 2; the remaining 7 multi-item scales from the KDQOL-SF: Supplementary Table S1) were all unchanged by the intervention.

Cost-Effectiveness

The mean (SD) of the area under the EQ-5D-5L curve was 0.665 (0.248) in the CON and 0.653 (0.269) in the intervention group. The mean difference between treatment and intervention groups obtained using the method of recycled predictions was −0.012 (95% CI: −0.069 to 0.043), suggesting no difference in QoL between the intervention and CONs (Figure 2 for an example analysis calculated using a low staff-to-patient ratio, outside London). No significant subgroup effects were found for age, sex, or diabetes at baseline.

Costs from different sources under different scenarios for staff costs are found in Table 3. Average total costs per patient in 6 months range from £232 (US$299) (95% CI: £204–£259) to £424 (US$546) (95% CI: £374–£474), depending on location and staff to patient ratio. The main cost factor was the staff cost for delivering the exercise sessions.

Effect of Intradialytic Exercise Training on Secondary Outcomes

Consistent with the lack of change in HRQoL, there were no statistically significant or absolute changes in physical function outcomes (Table 4), cardiovascular risk (arterial stiffness: Table 4), or clinical measures (routine clinical blood tests and medications: data not found). Although mortality was not influenced by the intervention, the number of hospitalizations tended to be higher in the EX group (Table 5). This trend was driven by 11 patients in the EX group who were each hospitalized more than 4 times during the trial for reasons deemed unlikely to be related to the intervention (e.g., fistula issues); in contrast, only 2 patients in the CON group were hospitalized more than 4 times.

Harms

There was no noticeable increase in SAEs in the exercise group (Table 6). Nevertheless, there was 1 noticeable SAE: an individual with type 1 diabetes and autonomic neuropathy experienced severe episodes of symptomatic hypotension that were possibly exacerbated by the intervention. The participant was withdrawn.

Compliance and Adherence (Fidelity) to the Exercise Prescription

A median (interquartile range) of 47 (28–77)% of exercise training sessions prescribed was completed by participants in EX. Nevertheless, only 18% of patients adhered exactly to the prescribed exercise type, intensity, and duration. Moreover, during the 6-month observation period, only 42% of participants avoided temporary cessation of the exercise intervention (Table 7). Reasons reported were fatigue and intercurrent medical events (Figure 3).

DISCUSSION

The aim of the PEDAL trial was to evaluate the clinical value of a 6-month intradialytic exercise program on QoL, compared with usual care, for patients receiving HD therapy. The PEDAL trial was novel in that it was the first to evaluate intradialytic exercise as would most likely be implemented, should health service commissioners include exercise training as part of the service

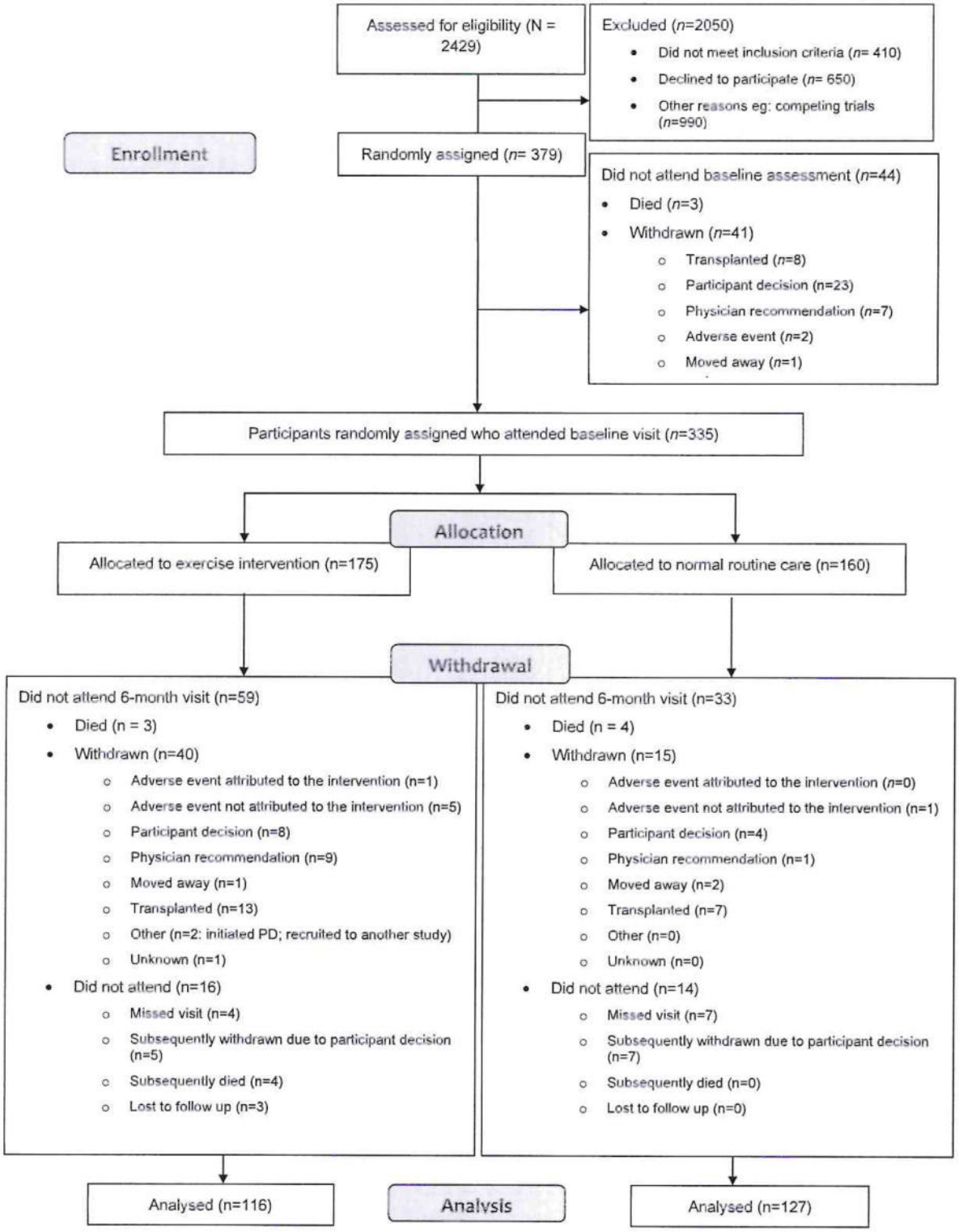

Figure 1. CONSORT diagram of the flow of patients across the various phases of the trial. CONSORT, Consolidated Standards of Reporting Trials; PD, progression disease.

specification for in-center HD. Unfortunately, as delivered, the PEDAL program did not statistically improve HRQoL, as assessed by the KDQOL-SF 1.3 PCS ($P = 0.055$), nor did it statistically improve QoL as assessed by the prespecified secondary outcomes of EQ-5D-5L, EQ-5D visual analog scale, or the

Table 1. Baseline characteristics of all patients in the trial, stratified by group, and according to withdrawal from the trial

	CON, not withdrawn		EX, not withdrawn		CON, withdrawn		EX, withdrawn	
Baseline characteristic	***N***	**Summary**	***N***	**Summary**	***N***	**Summary**	***N***	**Summary**
Age								
Mean (SD)	145	59.8 (14.1)	135	60.5 (15.0)	15	52.8 (19.9)	40	56.8 (13.3)
Median (Q1, Q3)		59.7 (50.5, 71.0)		62.1 (47.9, 72.9)		56.1 (34.7, 61.2)		56.3 (49.6, 64.3)
Gender								
n (%) Female	145	55 (38)	135	56 (42)	15	4 (27)	40	11 (28)
Ethnicity								
n (%) White	145	67 (46)	135	73 (54)	15	10 (67)	40	19 (48)
n (%) Black Caribbean		26 (18)		17 (13)		1 (7)		3 (8)
n (%) Black African		33 (23)		24 (18)		1 (7)		10 (25)
n (%) South Asian		15 (10)		16 (129)		2 (13)		6 (15)
n (%) Chinese		1 (1)		1 (1)		0 (0)		0 (0)
n (%) Other[a]		3 (2)		4 (3)		1 (7)		2 (5)
Weight (kg)								
Mean (SD)	143	80.8 (20.5)	135	79.2 (18.8)	15	82.5 (13.8)	40	82.8 (24.8)
Median (Q1, Q3)		77.0 (66.1, 92.2)		76.4 (65.4, 90.8)		83.0 (67.5, 91.5)		78.5 (67.4, 90.7)
BMI (kg/m^2)								
Mean (SD)	143	28.8 (6.5)	135	28.5 (6.5)	15	28.8 (5.5)	40	29.2 (8.8)
Median (Q1, Q3)		28.0 (24.5, 32.0)		27.0 (23.8, 32.2)		27.8 (24.2, 32.4)		27.6 (22.3, 32.6)
Smoking								
n (%) Current	145	19 (13.1)	135	18 (13.3)	15	0 (0.0)	40	5 (12.5)
n (%) Former		45 (31.0)		39 (28.9)		4 (26.7)		10 (25.0)
n (%) Never		81 (55.9)		78 (57.8)		11 (73.3)		25 (62.5)
SBP (mm Hg)								
Mean (SD)	142	138.6 (23.4)	135	134.4 (21.3)	15	133.9 (22.6)	40	134.1 (17.5)
Median (Q1, Q3)		138.0 (121.8, 153.9)		133.7 (121.3, 147.5)		130.0 (115.0, 152.2)		131.5 (121.0, 142.8)
DBP (mm Hg)								
Mean (SD)	142	73.4 (13.7)	135	72.6 (15.4)	15	75.5 (15.4)	40	76.9 (10.0)
Median (Q1, Q3)		73.3 (63.2, 81.7)		71.3 (61.3, 82.7)		74.0 (67.0, 80.7)		76.8 (70.8, 81.5)
Peripheral vascular disease								
n (%) Yes	145	6 (4.1)	135	5 (3.7)	15	0 (0.0)	40	0 (0.0)
Diabetes								
n (%) Yes	145	59 (40.7)	135	52 (38.5)	15	6 (40.0)	40	15 (37.5)
Hypertension								
n (%) Yes	145	116 (80.0)	135	101 (74.8)	15	11 (73.3)	40	33 (82.5)
Hyperlipidemia								
n (%) Yes	145	39 (26.9)	135	23 (17.0)	15	4 (26.7)	40	5 (12.5)
Previous MI								
n (%) Yes	145	21 (14.5)	135	14 (10.4)	15	0 (0.0)	40	6 (15.0)
Heart failure								
n (%) Yes	145	17 (11.7)	135	14 (10.4)	15	0 (0.0)	40	1 (2.5)
Cerebrovascular events								
n (%) Yes	145	17 (11.7)	135	8 (5.9)	15	1 (6.7)	40	0 (0.0)
Cardiovascular								
n (%) Yes	145	25 (17.2)	135	30 (22.2)	15	2 (13.3)	40	12 (30.0)
Musculoskeletal and orthopedic condition								
n (%) Yes	145	19 (13.1)	135	16 (11.9)	15	1 (6.7)	40	7 (17.5)
Hb								
Mean (SD)	141	110.2 (12.1)	127	109.8 (14.1)	15	118.1 (14.2)	37	108.9 (15.8)
Median (Q1, Q3)		109.0 (103.0, 119.0)		110.0 (102.0, 118.5)		115.0 (109.0, 124.0)		110.0 (100.0, 120.0)
CRP (mg/l)								
Mean (SD)	139	15.3 (21.1)	125	11.9 (15.9)	15	12.5 (16.4)	36	21.1 (26.6)
Median (Q1, Q3)		6.6 (3.1, 18.1)		6.0 (3.0, 14.1)		8.0 (4.5, 11.0)		10.9 (4.3, 28.1)
Dialysis efficiency (%)								
Mean (SD)	141	71.2 (8.4)	125	71.9 (7.3)	15	71.0 (11.3)	37	71.6 (7.9)
Median (Q1, Q3)		72.0 (66.0, 77.0)		73.0 (69.0, 76.5)		74.0 (68.0, 77.8)		71.8 (66.0, 77.0)

BMI, body mass index; CON, control group; CRP, C-reactive protein; DBP, diastolic blood pressure; EX, exercise intervention group; Hb, hemoglobin; MI, myocardial infraction; Q, quartile; SBP, systolic blood pressure.
Continuous variables are revealed as mean (SD) and median (Q1, Q3).
[a]Indian, Pakistani, and Bangladeshi.

Table 2. Response of quality of life to the PEDAL intervention, as assessed by KDQOL-SF 1.3 and EQ-5D-5L questionnaires

Outcome measure	n^a	Baseline	Month 6	Adjusted mean difference in change between EX and CON groups[b]	*P* value[c]
Primary outcome					
KDQOL-SF 1.3 PCS (AU)					
CON	120	32.9 (11.3)	31.8 (11.3)	2.4 (−0.1 to 4.8)	0.06
EX	114	33.8 (10.6)	34.8 (11.6)		
Secondary outcomes					
KDQOL-SF 1.3 Energy/fatigue (AU)					
CON	122	39.8 (26.0)	41.4 (24.9)	0.1 (−6.6 to 5.8)	0.97
EX	114	40.3 (27.2)	41.4 (26.4)		
KDQOL-SF 1.3 burden of kidney disease (AU)					
CON	122	36.0 (28.6)	37.3 (29.7)	−1.4 (−7.0 to 4.1)	0.61
EX	113	37.3 (27.7)	36.9 (29.0)		
EQ-5D-5L health utility score (AU)					
CON	121	0.69 (0.25)	0.68 (0.26)	0.01 (−0.04 to 0.07)	0.69
EX	111	0.71 (0.22)	0.70 (0.25)		
EQ-5D visual analog scale (0–100 scale)					
CON	121	59.4 (22.7)	59.3 (20.9)	3.5 (−1.0 to 8.1)	0.13
EX	111	60.7 (22.2)	63.7 (19.3)		

AU, arbitrary unit; CON, control group; EQ-5D, EuroQol 5-dimension descriptive system; EX, exercise intervention group; KDQOL-SF 1.3, Kidney Disease Quality of Life Short-Form; PCS, physical component summary; PEDAL, PrEscription of intraDialytic exercise to improve quAlity of Life.
[a]Number of participants with baseline and 6-month data available.
[b]Adjusting for baseline data and the randomization minimization variables (age, gender, diabetes status).
[c]Comparison between the control and intervention groups using a normal linear model.
Data are mean (SD) or mean (95% confidence interval). CON—usual care maintenance hemodialysis. EX—intradialytic exercise training plus usual care maintenance hemodialysis.

KDQOL-SF 1.3 multi-item scales of energy/fatigue and burden of kidney disease (Table 2).

The lack of statistical improvement in the PCS can be explained in part by the PEDAL participants having poor compliance (only 47% of prescribed exercise sessions were completed) and very poor adherence (only 18% of patients adhered to the prescribed progression of overload regarding type, intensity, and duration of exercise) to the exercise intervention. By design, the PEDAL trial aimed to have inclusive inclusion criteria. Consequently, baseline peak aerobic capacity values of 12 ml/min/kg were considerably lower than typically reported in previous studies (approximately 18 ml/min/kg).[10,12,18] This observation, combined with extremely low scores in physical performance (sit-to-stand and gait speed tests), confirms that the PEDAL cohort consisted of participants with severely low functional capacity. Arguably, this makes the PEDAL cohort more representative and its findings generalizable to the current HD population. Nevertheless, perhaps including such participants prevented benefits of the exercise intervention being realized in the relatively short 6-month intervention, and it is possible that some of these highly compromised participants may require a slower rate of overload progression and adaptation/adjustment periods to an aerobic intradialytic exercise intervention. Poor compliance and adherence to implemented renal exercise programs in clinical practice is well documented, with more than 50% of the patients starting exercise reportedly dropping out by 6 months, often owing to fatigue and being unwell.[18,37,38]

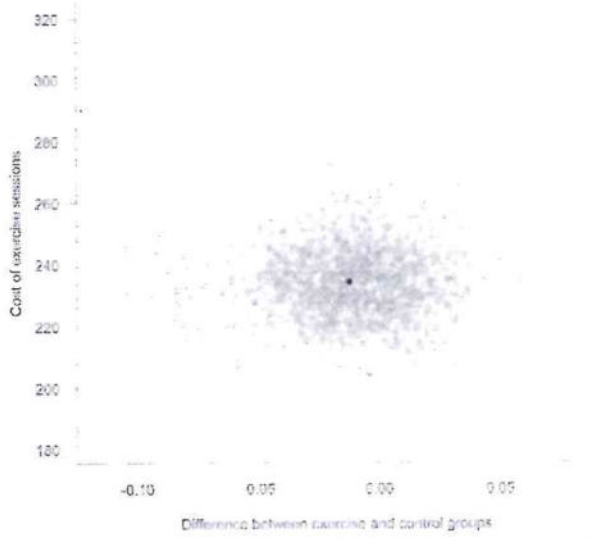

Figure 2. Cost-effectiveness: estimated differences in cost and QALYs on the ICER plane for a low staff-to-patient ratio, outside London (5000 bootstrap samples). ICER, incremental cost effectiveness ratio; QALY, quality-adjusted life year.

That the PEDAL program was not effective to increase PCS warrants comparison with previous studies. A Cochrane review completed in 2011 concluded that exercise was beneficial for HRQoL in patients with CKD, but unfortunately no meta-analysis or risk of bias assessment was performed, and many of the included studies were not representative of the HD population.[9] Other reviews have concluded positive effects of

Table 3. Costs per patient to deliver the PEDAL intervention in the 6-month follow-up period

Cost source	Outside London		London	
	Low staff-to-patient ratio	High staff-to-patient ratio	Low staff-to-patient ratio	High staff-to-patient ratio
Equipment purchasing and maintenance (£)	9 (8–10)	9 (8–10)	9 (8–10)	9 (8–10)
Staff delivering exercise sessions (£)	204 (180–228)	341 (300–381)	237 (209–265)	395 (348–441)
Training and oversight (£)	18 (16–20)	18 (16–20)	20 (18–23)	20 (18–23)
Total cost per patient in 6 months (£)	232 (204–259)	368 (324–412)	266 (235–298)	424 (374–474)
Estimated difference in cost (recycled predictions) (£)	234 (209–260)	372 (331–414)	269 (240–299)	428 (380–476)

PEDAL, PrEscription of intraDialytic exercise to improve quAlity of Life.
Data are mean (95% confidence interval). Estimated differences in cost obtained by the method of recycled prediction in 5000 bootstrap samples, setting cost in the control group to 0, adjusted for age, sex, and diabetes at baseline.

exercise but not on PCS[16,21,38] or have relied on studies at high risk of bias and with considerable heterogeneity.[17,20] Previous meta-analyses have also included extradialytic exercise programs[19,39,10] and intradialytic exercise programs that were intensively supervised (e.g., Ouzouni *et al.*[41]) or studies that have delivered progressive resistance training as opposed to aerobic cycling alone.[10,15,42] In this regard, 1 meta-analysis[22] usefully compared aerobic versus progressive resistance training versus combined exercise; only progressive resistance training increased PCS. Detailed analysis of the very few empirical studies included in reviews that do reveal positive effects of aerobic intradialytic exercise on QoL reveals that they have often used interventions that would be difficult to implement in routine care.[41] A recent study by Jeong *et al.*[43] found no significant improvements in physical function or QoL with a combined oral protein supplement and intradialytic cycling program. The authors suggested that a more comprehensive lifestyle management approach would be required to elicit improvements in these parameters. Taken together with the results reported herein, it is highly unlikely that clinically implementable intradialytic aerobic exercise

Table 4. Response of secondary outcome measures to the PEDAL intervention

Outcome measure	*n*[a]	Baseline	Month 6	Adjusted mean difference in change between EX and CON groups[b]	*P* value[c]
Peak aerobic capacity (VO_2 peak, l/min)					
CON	68	0.97 (0.38)	0.96 (0.37)	0.05 (−0.03 to 0.12)	0.22
EX	75	0.95 (0.42)	0.98 (0.43)		
Peak aerobic capacity (VO_2 peak, ml/min/kg)					
CON	68	11.9 (4.5)	11.8 (4.2)	0.75 (−0.20 to 1.71)	0.12
EX	74	11.8 (5.3)	12.4 (5.7)		
Arterial stiffness by pulse wave velocity (m/s)[27]					
CON	78	8.10 (6.78, 9.29)	7.78 (6.97, 9.13)	1.01 (0.97–1.06)	0.54
EX	78	7.92 (6.62, 9.09)	7.88 (6.98, 9.27)		
DASI (AU)					
CON	121	23.1 (13.1)	22.7 (13.4)	0.35 (−2.23 to 2.93)	0.79
EX	112	24.9 (13.3)	24.1 (14.3)		
IPAQ total physical activity (MET, min/wk) [ln(x + 10)]					
CON	118	423.8 (39.0, 1465.4)	353.2 (46.1, 1033.1)	1.36 (0.84–2.21)	0.21
EX	106	709.5 (153.8, 2515.1)	591.0 (111.8, 1793.2)		
Gait speed in 10 m (m/s)					
CON	84	0.86 (0.30)	0.87 (0.29)	0.01 (−0.04 to 0.06)	0.73
EX	79	0.94 (0.29)	0.94 (0.30)		
Sit-to-stand 60 s (no. of repetitions)					
CON	87	13.8 (6.6)	14.4 (7.0)	1.02 (−0.42 to 2.47)	0.16
EX	82	15.8 (7.1)	17.1 (8.1)		
Tinetti Falls Efficacy Scale (AU) [ln(x)]					
CON	122	22.5 (10.2, 46.8)	24.5 (11.0, 50.0)	0.94 (0.80–1.12)	0.49
EX	112	23.0 (11.8, 49.2)	24.5 (11.0, 46.2)		

AU, arbitrary units; CON, control group; DASI, Duke Activity Status Index; EX, exercise intervention group; IPAQ, International Physical Activity Questionnaire; MET, metabolic equivalent task; PEDAL, PrEscription of intraDialytic exercise to improve quAlity of Life; VO2, maximum rate of oxygen consumption.
[a]Number of participants with baseline and 6-month data available.
[b]Adjusting for baseline data and the randomization minimization variables (age, gender, diabetes status): note variables analyzed as log-transformed values are given as ratios.
[c]Comparison between the control and intervention groups using a normal linear model.
Data are mean (SD), median (IQR), or mean (95% confidence interval); some variables were transformed to enhance model fit: transformations are given in [brackets]. CON—usual care maintenance hemodialysis; EX—intradialytic exercise training plus usual care maintenance hemodialysis.

Table 5. Number of hospitalizations and mortality during the PEDAL trial

Variable	n[a]	No. of hospitalizations (hospitalization rate per person year)	[b]Incident rate ratio (95% confidence interval)	P value[c]
No. of hospitalizations				
CON	160	84 (0.54)	1.39 (0.93–2.08)	0.109
EX	175	132 (0.85)		
		No. of events (event rate per 100 person years)	[d]Hazard ratio (95% confidence interval)	P value
All-cause mortality				
CON	160	9 (5.8)	1.19 (0.48–2.94)	0.71
EX	174	10 (6.5)		
Cardiovascular mortality				
CON	160	3 (1.9)	N/A	N/A
EX	174	2 (1.3)		

CON, control group; EX, exercise intervention group; N/A, not applicable; PEDAL, PrEscription of intraDialytic exercise to improve quAlity of Life.
[a]Number of participants with baseline and 6-month data available.
[b]Incident rate ratios have been calculated in negative binomial regression predicting number of hospitalizations from treatment, adjusting for age, sex, and diabetes at baseline.
[c]For all-cause mortality, survival was adjusted for age, sex, and diabetes at baseline; for cardiovascular mortality, survival was adjusted for age and diabetes at baseline.
[d]Hazard ratios have been calculated in Cox proportional hazard regression models predicting survival from treatment.
CON—usual care maintenance hemodialysis. EX—intradialytic exercise training plus usual care maintenance hemodialysis. N/A—as numbers too small to analyze.

training alone can improve QoL at a whole population level.

In addition to evaluating potential benefits, the PEDAL study uniquely assessed the cost of delivery of its intervention by recording harms and using health economic methods. The number of hospitalizations, all-cause mortality, and cardiovascular mortality was not noticeably different between the groups. Although these results should be interpreted cautiously owing to the low number of events, there was no increase in SAE in the exercise group either. The economic cost of delivering the PEDAL intervention ranged from £464 (US$598) to £848 (US$1092) per participant per year (depending on pay band of the physiotherapy assistant, whether London weighting was applied, and staff-to-patient ratio). Note this calculation assumed that physiotherapy assistants supervised between 6 and 10 participants per dialysis session without incurring any travel costs and that exercise would be offered as part of a general physiotherapy service (with enough capacity to provide absence cover at no additional cost). It also assumes that patients will only exercise for between 1 and 2 sessions per week (the calculation is based on compliance to the PEDAL intervention, which was only 47%). For comparison purposes, the cost of delivering cardiac rehabilitation is £477 (US$614) per person per year,[44] equating to costs of £550 (US$709) to £12,558 (US$16,178) per quality-adjusted life year gained.[45] In contrast, PEDAL had no apparent QoL gain, albeit in a relatively short period of observation of 6 months (cost-effectiveness of rehabilitation programs increases with time[44,45]). The cost of delivery of HD in the UK is approximately £35,000 (US$45,088) per patient per year.[46] As the PEDAL trial was

Table 6. Number of patients with at least 1 SAE by MedDRA system organ class during the PEDAL trial

Variable	All, n (%)	CON, n (%)	EX, n (%)
Number of randomized patients who attended baseline visit	335	160	175
Number of patients with any event	125	56 (35.0)	69 (39.4)
Blood and lymphatic system disorders	2 (0.6)	0 (0.0)	2 (1.1)
Cardiac disorders	15 (4.5)	6 (3.8)	9 (5.1)
Congenital, familial, and genetic disorders	1 (0.3)	1 (0.6)	0 (0.0)
Gastrointestinal disorders	14 (4.2)	4 (2.5)	10 (5.7)
General disorders and administration site conditions	17 (5.1)	12 (7.5)	5 (2.9)
Hepatobiliary disorders	3 (0.9)	1 (0.6)	2 (1.1)
Infections and infestations	47 (14.0)	18 (11.2)	29 (16.6)
Injury, poisoning, and procedural complications	28 (8.4)	12 (7.5)	16 (9.1)
Investigations	5 (1.5)	4 (2.5)	1 (0.6)
Metabolism and nutrition disorders	17 (5.1)	4 (2.5)	13 (7.4)
Musculoskeletal and connective tissue disorders	4 (1.2)	1 (0.6)	3 (1.7)
Neoplasms benign, malignant and unspecified (including cysts and polyps)	1 (0.3)	0 (0.0)	1 (0.6)
Nervous system disorders	8 (2.4)	3 (1.9)	5 (2.9)
Psychiatric disorders	4 (1.2)	1 (0.6)	3 (1.7)
Renal and urinary disorders	1 (0.3)	1 (0.6)	0 (0.0)
Reproductive system and breast disorders	2 (0.6)	1 (0.6)	1 (0.6)
Respiratory, thoracic and mediastinal disorders	13 (3.9)	3 (1.9)	10 (5.7)
Skin and subcutaneous tissue disorders	1 (0.3)	0 (0.0)	1 (0.6)
Social circumstances	1 (0.3)	1 (0.6)	0 (0.0)
Surgical and medical procedures	37 (11.0)	13 (8.1)	24 (13.7)
Vascular disorders	10 (3.0)	6 (3.8)	4 (2.3)

CON, control group; EX, exercise intervention group; MedDRA, Medical Dictionary for Regulatory Activities; PEDAL, PrEscription of intraDialytic exercise to improve quAlity of Life; SAE, serious adverse event.
CON—usual care maintenance hemodialysis. EX—intradialytic exercise training plus usual care maintenance hemodialysis.

Table 7. Summary of exercise compliance and adherence to the PEDAL trial intervention during the 6-month follow-up period

Compliance (percentage of expected sessions completed)	
Sample size (n)	175
Median (IQR)	47 (28–77)
Temporary (>2 wk) cessation of exercise	
Sample size (n)	119
n (%)	69 (58)
Adhered (fidelity to type/intensity/duration) to the exercise prescription	
Sample size (n)	119
n (%)	21 (18)

IQR, interquartile range; PEDAL, PrEscription of intraDialytic exercise to improve quAlity of Life.

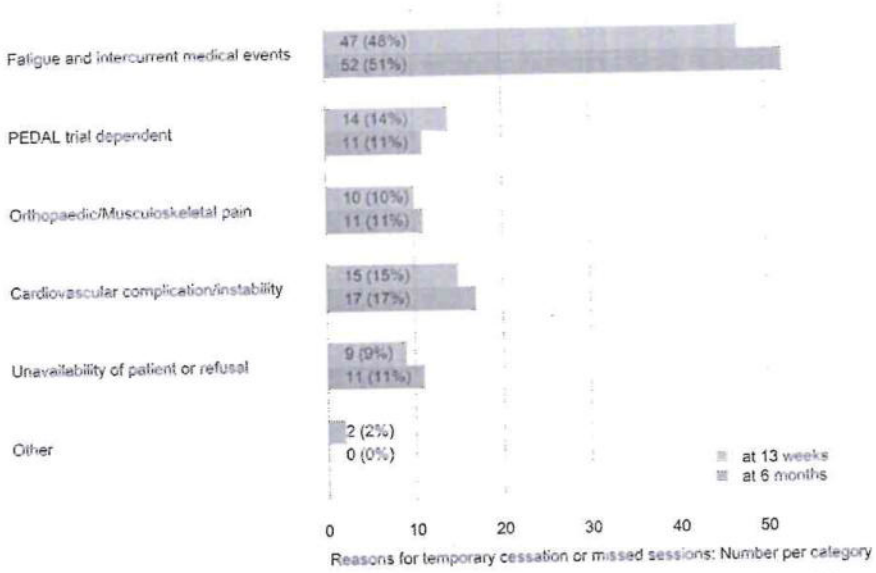

Figure 3. Number (%) of recorded incidents of temporary cessation (>2 weeks) or missed exercise sessions with reasons.

not clinically effective at a whole sample level, whether the cost of delivery of intradialytic exercise is justified to enhance patient choice remains a matter for debate.

Limitations

PEDAL was designed to assess a pragmatic, clinically implementable intradialytic exercise intervention. By design, the study relied on a patient-reported outcome measure for its primary outcome; it is recognized that the primary limitation of this study was the lack of an attention CON. In this regard, it is possible that an experimenter effect explains the 2.4 arbitrary unit increase (albeit nonsignificant) in PCS.[47] This interpretation is supported by the lack of absolute or statistical changes in objective measures of physical function, cardiovascular risk, and clinical measures (Table 2), consistent with a conclusion that intradialytic aerobic exercise *per se* had no clinical benefit. In addition, the study was not powered to detect differences in some secondary outcomes, including mortality. Nevertheless, we reported these data to allow a balance of benefits and harms to be evaluated. Future studies should address these concerns by including attention control arms and being adequately powered for all outcome measures. Perhaps the most important finding of the PEDAL study was the observation of poor compliance and adherence when intradialytic exercise was implemented as part of routine care. It is acknowledged that the lack of absolute or significant change in objective measures may in part be due to limitations in the effective implementation of delivering an adequate dose of exercise stimulus as indicated by the very low compliance and adherence data. PEDAL was designed to be a pragmatic intervention, and no additional strategies to address low compliance or adherence were introduced. Thus, future studies need to evaluate whether there are subgroups of patients who may benefit from this type of intervention and whether there is scope to optimize strategies to improve compliance and adherence with intradialytic cycling interventions, implementation settings, and resources to deliver exercise-based interventions to improve effectiveness.

CONCLUSIONS

The PEDAL study was a rehabilitation program that could realistically be commissioned as part of routine care. Compliance and adherence with the exercise intervention, as per the study design, were extremely low. In this inclusive sample of people on HD, many of whom were severely deconditioned; the findings therefore suggest that 6 months of intradialytic aerobic exercise did not improve HRQoL.

DISCLOSURE

All the authors declared no competing interests.

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AUTHOR CONTRIBUTIONS

SAG, PK, JHM, ICM, IF, AS, and TM conceived and designed the study; IF and CMM analyzed the data; SAG, JHM, and PK interpreted and contextualized the data and drafted the paper; SAG, JHM, PK, DW, SB, KF, MT, PAK, MK, JB, ICM, IF, CMM, SK, CR, IDG, CR, MY, PT, SM, TM, and AS revised the paper; all authors approved the final manuscript.

SUPPLEMENTARY MATERIAL

Supplementary File (PDF)

Table S1. Response of quality of life to the PEDAL intervention, as assessed by the Kidney Disease Quality of Life Short-Form (KDQOL-SF 1.3) multi-item scales.

Consort checklist.

STROBE Statement.

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