

Isothermic Versus Standard-Temperature Dialysis: Impact on Blood Pressure Variability, Headache and Recovery Time

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Abstract:

Background: Intradialytic hypertension (IDH) affects a meaningful share of people on maintenance haemodialysis and is linked to higher hospitalisation and mortality. Heat gained from a standard 37.0 °C dialysate may drive this rise in blood pressure, yet the idea has rarely been tested in haemodynamically stable patients.

Objective: To compare the incidence of IDH, intradialytic hypotension and neurological symptoms during isothermic versus standard-temperature haemodialysis.

Methods: In this prospective, single-centre, randomised crossover study, 72 stable adults each completed four sessions: two with dialysate at 37.0 °C and two with dialysate matched to tympanic core temperature, rechecked hourly. Blood pressure was recorded every 15 minutes. IDH was defined as a systolic rise of at least 10 mmHg from pre- to post-dialysis. Session-level outcomes were analysed with generalised estimating equations and linear mixed models.

Results: The mean isothermic dialysate temperature was 36.4 ± 0.3 °C. IDH occurred in 58 of 144 standard sessions (40.3%) and 27 of 144 isothermic sessions (18.8%) (odds ratio 2.92; 95% CI 1.71–4.99). Intradialytic hypotension fell from 21.5% to 8.3%, and headache from 15.3% to 6.3%. Time-averaged systolic pressure was 5.4 mmHg lower, within-session systolic variability was smaller (11.8 ± 3.6 vs 16.9 ± 5.1 mmHg; $p < 0.001$), and post-dialysis recovery time was halved.

Conclusion: Matching dialysate temperature to core body temperature reduced both hypertensive and hypotensive episodes and eased symptom burden, pointing to heat gain as a modifiable cause of blood pressure instability during dialysis.

Keywords: Haemodialysis; Intradialytic hypertension; Isothermic dialysis; Dialysate temperature; Blood pressure variability; Intradialytic headache

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Introduction

Haemodialysis keeps millions of people with kidney failure alive, but every session places a real burden on the circulation. Several litres of fluid are removed within a few hours, solutes shift rapidly, and blood is pumped through an external circuit. In most patients these changes lower blood pressure. A smaller group behaves in the opposite way: their pressure climbs during treatment and is often higher at the end of the session than at the start. This pattern is called intradialytic hypertension (IDH). Definitions vary, but the most widely used one is a rise in systolic blood pressure of 10 mmHg or more from pre- to post-dialysis, and reported prevalence usually lies between 5% and 15% [1].

IDH was once treated as a curiosity, but it is now clear that it carries prognostic weight. In a secondary analysis of incident patients, each 10 mmHg increase in systolic pressure during dialysis was

associated with a higher risk of death over two years [2]. A similar link with hospitalisation and mortality has been shown in prevalent patients [3]. These observations have encouraged clinicians to look more closely at why pressure rises in some people and not in others.

Several mechanisms have been proposed. Hidden volume overload, sympathetic overactivity, activation of the renin–angiotensin system, removal of water-soluble antihypertensive drugs and high dialysate calcium all appear to play a part [1]. Studies of vascular physiology have shown a rise in peripheral resistance during sessions complicated by IDH [4], together with endothelial dysfunction and an imbalance between endothelin-1 and nitric oxide [5].

Temperature is a less familiar, but plausible, contributor. Blood leaving the body cools in the extra-

corporeal circuit and is then rewarmed by dialysate that is usually set at 37.0 °C. Because many dialysis patients have a core temperature below this value, the net effect is heat transfer into the body and a gradual rise in core temperature during treatment [6]. Isothermic dialysis aims to remove this heat load by keeping core temperature stable, an approach that is technically achievable with simple adjustments [7]. Controlling thermal balance improved vascular stability in a European randomised trial [8], and systematic reviews have confirmed that cooler dialysate reduces intradialytic hypotension [9,10].

The same question matters to the brain. Cooler dialysate protected cerebral white matter from progressive damage in a randomised trial [11], and falls in blood pressure during dialysis are associated with measurable cerebral ischaemia [12]. Unstable blood pressure in either direction may therefore affect cognition, headache and post-dialysis fatigue, symptoms that patients often rank among their greatest concerns.

Almost all cooling studies have focused on hypotension-prone patients, and very little is known about how isothermic dialysis affects blood pressure rises in stable patients. We therefore designed a randomised crossover study to test whether matching dialysate temperature to each patient's core temperature reduces the incidence of IDH. Secondary aims were to examine intradialytic hypotension, blood pressure variability and neurological symptoms such as intradialytic headache and delayed recovery after treatment.

Materials and Methods

Study Design and Ethics: This was a prospective, single-centre, randomised crossover study carried out in the haemodialysis unit of a tertiary care teaching hospital over 12 months. The institutional ethics committee approved the protocol, and every participant gave written informed consent before enrolment.

Participants: Adults aged 18 years or older who had received maintenance haemodialysis for at least three months through an arteriovenous fistula or graft were eligible. Participants had to be clinically euvolaemic with a stable dry weight and predialysis blood pressure below 170/100 mmHg, and their antihypertensive regimen had to be unchanged for at least two weeks. We excluded patients with fever or infection in the preceding month, heart failure of New York Heart Association class III or IV, active malignancy, recent stroke or seizure, thyroid disease, or a tunnelled catheter as the only access.

Intervention and Randomization: Each patient completed four study sessions within four consecutive weeks: two at a standard dialysate temperature

of 37.0 °C and two isothermic sessions. The order was assigned by computer-generated block randomisation. For isothermic sessions, tympanic temperature was measured with an infrared thermometer immediately before cannulation, and dialysate temperature was set to the same value. Tympanic temperature was rechecked every hour, and the dialysate was adjusted if core temperature had changed by 0.2 °C or more. All four sessions were scheduled at the same time of day to reduce circadian variation, with the room kept at 24–26 °C.

Dialysis Prescription: All sessions lasted four hours using low-flux polysulfone dialysers and bicarbonate dialysate (sodium 138 mmol/L, potassium 2.0 mmol/L, calcium 1.25 mmol/L). Blood flow was 250–300 mL/min, dialysate flow was 500 mL/min, and unfractionated heparin was used for anticoagulation. Dry weight, ultrafiltration targets and medications were not altered during the study.

Outcomes and Data Collection: Blood pressure and pulse were recorded with a validated automated oscillometric device before dialysis, every 15 minutes during treatment and at the end of the session. The primary outcome was IDH, defined as a rise in systolic pressure of at least 10 mmHg from pre- to post-dialysis. Secondary outcomes included intradialytic hypotension (a fall in systolic pressure of at least 20 mmHg with symptoms, or any systolic value below 90 mmHg), time-averaged systolic pressure, within-session standard deviation of systolic pressure, change in core temperature, intradialytic headache, muscle cramps and shivering. Recovery time was recorded with the standard question, "How long does it take you to recover from a dialysis session?", asked the next day.

Statistical Analysis: A sample of 72 patients (144 sessions per arm) was estimated to give 80% power to detect a reduction in IDH from 40% to 23% at a two-sided alpha of 0.05, allowing for within-patient correlation. Continuous data are shown as mean $\pm$ standard deviation or median with interquartile range, and categorical data as counts and percentages. Binary session outcomes were compared using generalised estimating equations with an exchangeable correlation structure, and continuous outcomes with linear mixed-effects models including patient as a random effect and period as a fixed effect. A p value below 0.05 was considered significant. Analyses were performed with SPSS version 26.

Results

Of 96 patients screened, 72 were enrolled and completed all four study sessions, giving 144 standard and 144 isothermic sessions for analysis. No patient withdrew, and no session was stopped early. The mean dialysate temperature during isothermic sessions was 36.4 ± 0.3 °C (range 35.8–

37.0 °C), a separation of 0.6 °C from standard sessions.

Table 1: Baseline demographic and clinical characteristics of the study population (n = 72)

Characteristic	Value (n = 72)
Age (years)	54.2 ± 11.8
Male sex	49 (68.1)
Diabetes mellitus	34 (47.2)
Primary kidney disease: diabetic nephropathy	30 (41.7)
Primary kidney disease: hypertensive nephrosclerosis	18 (25.0)
Primary kidney disease: chronic glomerulonephritis	12 (16.7)
Primary kidney disease: other or unknown	12 (16.7)
Dialysis vintage (years)	3.1 ± 1.9
Thrice-weekly schedule	52 (72.2)
AVF as vascular access	67 (93.1)
Body mass index (kg/m ²)	23.8 ± 3.6
Interdialytic weight gain (kg)	2.9 ± 1.1
Residual urine output ≥200 mL/day	21 (29.2)
Pre-dialysis systolic BP (mmHg)	146.8 ± 12.4
Pre-dialysis diastolic BP (mmHg)	83.5 ± 9.2
Number of antihypertensive drugs	2.1 ± 0.8
Haemoglobin (g/dL)	9.8 ± 1.4
Serum albumin (g/dL)	3.6 ± 0.4
eKt/V	1.32 ± 0.21
Pre-dialysis tympanic temperature (°C)	36.4 ± 0.3
Pre-dialysis axillary temperature (°C)	36.0 ± 0.3

Values are mean ± SD or n (%). AVF: arteriovenous fistula; eKt/V: equilibrated Kt/V.

Table 1 summarises the baseline profile of the 72 participants. The group was middle-aged, with a mean age of 54.2 years, and just over two-thirds were men. Nearly half had diabetes, and diabetic nephropathy was the most common cause of kidney failure, followed by hypertensive nephrosclerosis.

Most patients dialysed three times a week through a native arteriovenous fistula, and the mean dialysis vintage was about three years. Pre-dialysis blood pressure was moderately raised despite an average of two antihypertensive drugs. Importantly, the mean tympanic temperature before dialysis was 36.4 °C, clearly below the conventional 37.0 °C dialysate setting, which confirms the potential for heat gain during standard treatment.

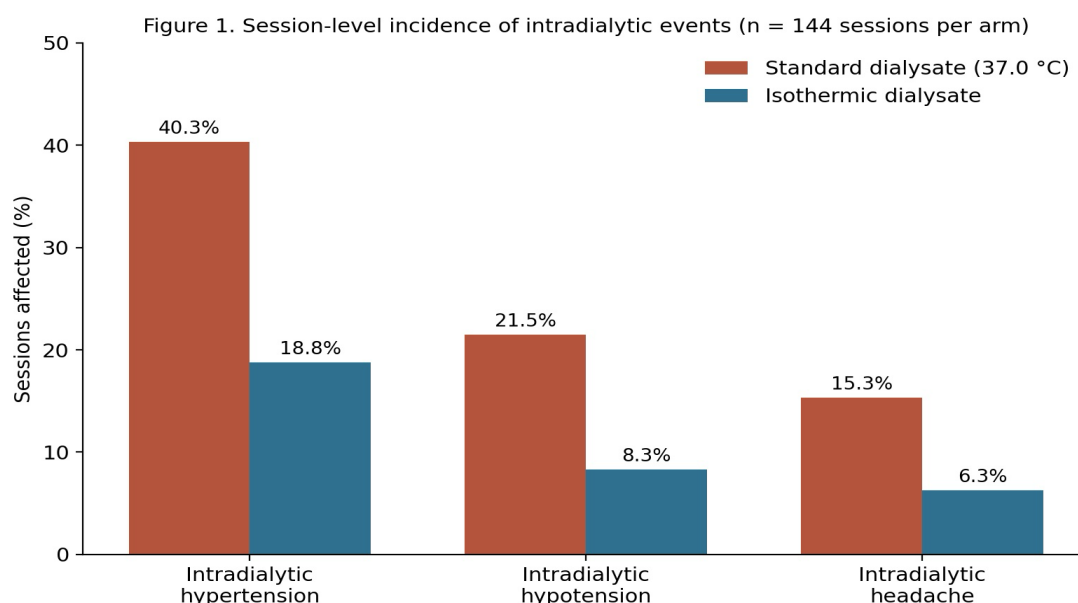


Figure 1: Incidence of intradialytic hypertension, hypotension and headache during standard and isothermic sessions

Figure 1 compares how often key intradialytic events occurred in each arm. IDH was recorded in 40.3% of standard sessions but in only 18.8% of isothermic sessions, meaning the odds of IDH were almost three times higher when dialysate was set at 37.0 °C (odds ratio 2.92; 95% CI 1.71–4.99). Cooling to core temperature did not simply trade one

problem for another: symptomatic hypotension also fell, from 21.5% to 8.3% (odds ratio 3.02; 95% CI 1.48–6.15). Intradialytic headache, a common neurological complaint, was reported in 15.3% of standard sessions and 6.3% of isothermic sessions (odds ratio 2.70; 95% CI 1.20–6.10).

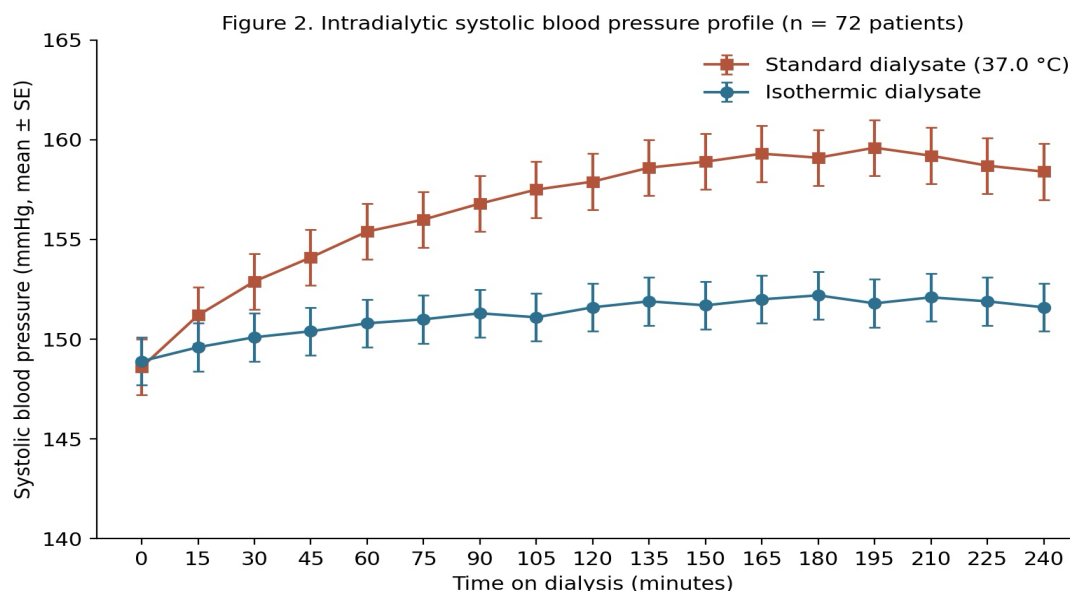


Figure 2: Mean systolic blood pressure recorded every 15 minutes across the 4-hour session

Figure 2 plots mean systolic blood pressure at each 15-minute interval. Pre-dialysis values were almost identical in both arms, which shows that the groups started from the same point. During standard sessions, systolic pressure rose steadily through the first two hours and reached a plateau of about 159 mmHg in the final hour. During isothermic ses-

sions, the curve stayed close to baseline and never exceeded 152.2 mmHg. The two lines separated within the first 30 minutes, and the gap widened as treatment went on. The time-averaged systolic pressure was 156.6 mmHg in standard sessions and 151.2 mmHg in isothermic sessions, a mean difference of 5.4 mmHg ($p < 0.001$).

Table 2: Session-level haemodynamic, thermal and symptom outcomes by dialysate temperature (144 sessions per arm)

Outcome	Standard (37.0 °C)	Isothermic	Difference or OR (95% CI)	P
Dialysate temperature (°C)	37.0 ± 0.0	36.4 ± 0.3	-0.6 (-0.65 to -0.55)	<0.001
Pre-dialysis SBP (mmHg)	147.1 ± 13.0	146.5 ± 12.7	-0.6 (-2.6 to 1.4)	0.54
Post-dialysis SBP (mmHg)	156.3 ± 15.9	147.2 ± 14.1	-9.1 (-11.6 to -6.6)	<0.001
Time-averaged SBP (mmHg)	156.6 ± 9.8	151.2 ± 8.9	-5.4 (-6.9 to -3.9)	<0.001
Within-session SD of SBP (mmHg)	16.9 ± 5.1	11.8 ± 3.6	-5.1 (-6.1 to -4.1)	<0.001
Rise in core temperature (°C)	0.52 ± 0.21	0.08 ± 0.17	-0.44 (-0.49 to -0.39)	<0.001
Ultrafiltration volume (L)	2.8 ± 0.9	2.8 ± 0.9	0.0 (-0.2 to 0.2)	0.87
Intradialytic hypertension, n (%)	58 (40.3)	27 (18.8)	OR 2.92 (1.71–4.99)	<0.001
Intradialytic hypotension, n (%)	31 (21.5)	12 (8.3)	OR 3.02 (1.48–6.15)	0.002
Intradialytic headache, n (%)	22 (15.3)	9 (6.3)	OR 2.70 (1.20–6.10)	0.02
Muscle cramps, n (%)	19 (13.2)	14 (9.7)	OR 1.41 (0.68–2.93)	0.36
Shivering or feeling cold, n (%)	3 (2.1)	8 (5.6)	—	0.13
Recovery time (minutes), median (IQR)	120 (60–240)	60 (30–150)	—	<0.001

Values are mean ± SD, n (%) or median (IQR). Differences are isothermic minus standard; odds ratios compare standard with isothermic sessions and were derived from generalised estimating equa-

tions. SBP: systolic blood pressure; SD: standard deviation.

Table 2 presents the session-level outcomes. Pre-dialysis pressure and ultrafiltration volume were

the same in both arms, so differences cannot be explained by fluid removal. Core temperature rose by about half a degree during standard sessions but stayed nearly flat with isothermic dialysate. This thermal difference was matched by lower post-dialysis and time-averaged systolic pressures. Hypertension, hypotension and headache were all less

frequent with isothermic dialysis, while cramps did not differ significantly. Shivering was slightly more common with cooler dialysate but remained rare and never led to early termination. Patients also reported recovering from treatment in roughly half the usual time.

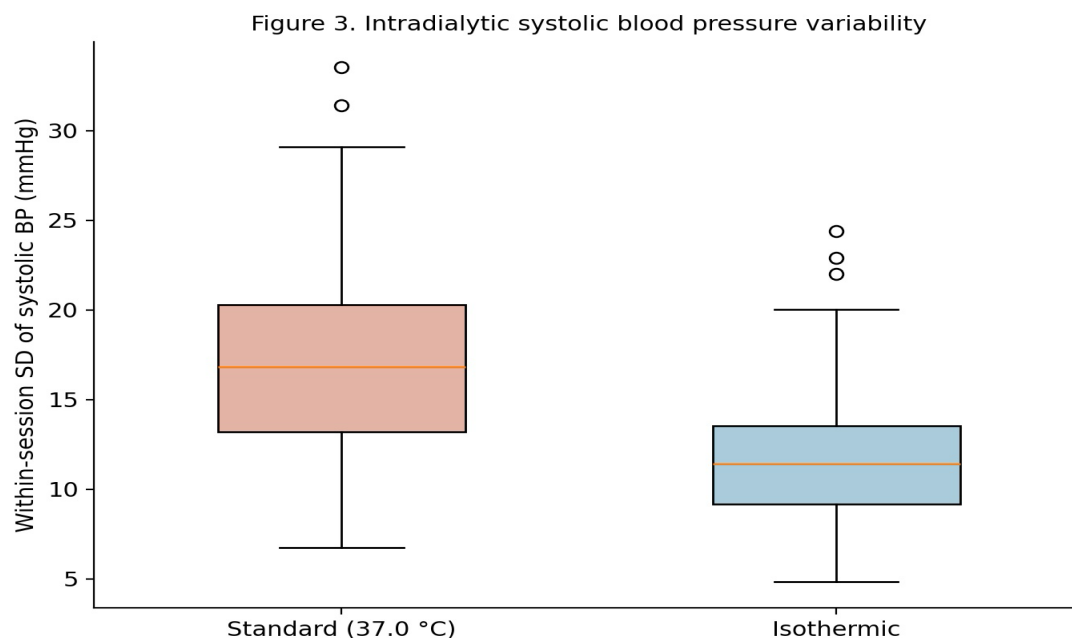


Figure 3: Within-session variability of systolic blood pressure in standard and isothermic sessions

Figure 3 shows the spread of within-session standard deviation of systolic pressure, a simple marker of how much blood pressure fluctuated during each treatment. Standard sessions had a mean variability of 16.9 ± 5.1 mmHg, and the upper whisker extended well beyond 25 mmHg, showing that some sessions were markedly unstable. Isothermic sessions had a lower mean of 11.8 ± 3.6 mmHg and a narrower interquartile range ($p < 0.001$). The reduction was seen across the whole distribution rather than being driven by a few outliers. Smoother blood pressure during dialysis is clinically relevant because repeated swings may harm the heart and the brain.

Discussion

This randomised crossover study shows that setting dialysate temperature to each patient's own core temperature more than halved the frequency of intradialytic hypertension in stable haemodialysis patients. The benefit did not come at the cost of more hypotension; in fact, hypotensive episodes, blood pressure variability, headache and recovery time all improved together. Because each patient acted as their own control and ultrafiltration was identical in both arms, the most likely explanation is the difference in heat balance.

Our finding that core temperature rose by about 0.5°C during standard sessions agrees with earlier thermal studies showing that 37.0°C dialysate delivers heat to most patients (6,7). Patients with kidney failure tend to have a lower baseline temperature than the general population, and a falling temperature trend has itself been linked with poorer outcomes [15]. A fixed dialysate setting therefore treats a heterogeneous group as if everyone were the same.

How could extra heat raise blood pressure when heat is usually thought of as a vasodilator? The answer probably lies in the combined stress of warming and fluid removal. Passive heat stress increases sympathetic outflow, redistributes blood away from the splanchnic bed and alters vascular responses to vasoconstrictors [16]. Heat also changes baroreflex control of sympathetic activity through central interaction between thermoregulatory and pressure-sensing pathways, independent of blood volume [17]. In patients prone to IDH, who already show exaggerated peripheral resistance and endothelial dysfunction [4,5], this sympathetic drive may dominate and push pressure upward. In hypotension-prone patients, the vasodilator response wins instead. Removing the heat load appears to calm both extremes, which may explain

why hypertension and hypotension fell together in our cohort.

IDH is not simply a rise seen at the end of a session. It is associated with higher interdialytic ambulatory pressure [13] and with endothelial abnormalities that respond to targeted treatment [18]. Recurrent circulatory stress during dialysis can injure the heart and other organs through repeated ischaemia [19]. Individualised cooling preserved left ventricular structure and function over one year in a randomised trial [14], and our results suggest that better intradialytic blood pressure control may be one route to that benefit.

The neurological findings deserve particular attention. Headache occurs frequently during dialysis and is often attributed to osmotic shifts, yet blood pressure surges and dips are also recognised triggers. Cooler dialysate slowed white matter injury in a randomised imaging study [11], and intradialytic hypotension has been linked to reduced cerebral oxygenation [12]. The lower rate of headache and the shorter recovery time we observed fit with the idea that steadier cerebral perfusion helps patients feel better after treatment. Recovery time is a patient-centred outcome that strongly influences quality of life.

Safety concerns about cooling usually centre on discomfort. Shivering was slightly more common with isothermic dialysate, but it was mild and uncommon, consistent with reviews showing good tolerance of modest cooling [9,20]. Fixed low temperatures of 36.0 °C have not consistently improved outcomes [21], supporting a personalised rather than uniform strategy. Isothermic dialysis requires only a thermometer and a machine setting, which makes it practical in resource-limited units. Larger multicentre trials with longer follow-up are now needed to test whether reduced IDH translates into fewer cardiovascular and neurological events.

This was a single-centre study with a short follow-up and a modest sample. Tympanic temperature was used as a surrogate for core temperature. Patients and staff could not be blinded to dialysate temperature. Dialysate–plasma sodium gradients, ambulatory interdialytic blood pressure and formal cognitive testing were not assessed.

Conclusion

Isothermic haemodialysis, in which dialysate temperature is matched to the patient's own core temperature, significantly reduced the incidence of intradialytic hypertension in stable patients. The same simple adjustment also lowered intradialytic hypotension, reduced blood pressure variability, decreased intradialytic headache and shortened post-dialysis recovery time, without changes in ultrafiltration. These findings suggest that heat gained from a standard 37.0 °C dialysate is a mod-

ifiable contributor to blood pressure instability during dialysis. Because the intervention is inexpensive and easy to implement, it deserves evaluation in larger multicentre trials that examine long-term cardiovascular, cognitive and survival outcomes.

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