

# Extended Septal Myectomy in Obstructive Hypertrophic Cardiomyopathy. Clinical Results and Mid-term Echocardiographic Outcome

## *Miectomía septal ampliada en la miocardiopatía hipertrófica obstructiva: resultados clínicos y evolución ecocardiográfica a mediano plazo*

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### ABSTRACT

**Background:** Extended septal myectomy is the treatment of choice for patients with symptomatic obstructive hypertrophic cardiomyopathy, refractory to pharmacological treatment.

**Objectives:** The aim of this study was to evaluate postoperative results, symptom changes and echocardiographic outcome in a population undergoing extended septal myectomy for symptomatic obstructive hypertrophic cardiomyopathy.

**Methods:** A total of 28 patients were operated on from November 2011 to October 2017. Postoperative, clinical and echocardiographic outcomes were analyzed at discharge and during follow-up.

**Results:** Mean age was  $53.3 \pm 13.4$  years. Perioperative mortality (<30 days) was 0%. One patient died 90 days after the procedure (3.5%). No septal defect, aortic valve injury or mitral valve replacement occurred in any patient. Ninety-one percent of patients were in FC III-IV, and the rest had angina or syncope. During follow-up, 92.8% were asymptomatic; one patient was in FC III and another in FC II. Preoperative basal average gradient was 53.5 mmHg and with Valsalva maneuver 86.4 mmHg, and postoperative basal and with Valsalva gradient was 9.4 mmHg and 13.5 mmHg, respectively ( $p < 0.01$ ). During follow-up, gradients at rest and with Valsalva were even lower: 8.3 mmHg and 10.7 mmHg, respectively ( $p$ : NS). Nine patients (32%) presented prior moderate to severe mitral regurgitation due to mitral valve systolic anterior motion or intrinsic disease. Only one patient had evidence of asymptomatic moderate mitral regurgitation at follow-up (3.5%). Median follow-up was 400 days (25-75 IQR: 695 days; minimum: 30 days and maximum: 1,868 days).

**Conclusion:** Extended septal myectomy improves hemodynamic and clinical outcome in symptomatic patients, with a low number of postoperative complications, resulting in better quality of life.

**Key Words:** Cardiomyopathy, Hypertrophic - Heart Septum/surgery - Heart Septum/diagnostic imaging - Cardiac Surgical Procedures/methods

### RESUMEN

**Introducción:** La miectomía septal ampliada constituye el tratamiento de elección para pacientes con miocardiopatía hipertrófica obstructiva sintomática, refractarios al tratamiento farmacológico.

**Objetivos:** Evaluar los resultados posoperatorios, el cambio en los síntomas y la evolución ecocardiográfica de una población sometida a miectomía septal ampliada por miocardiopatía hipertrófica obstructiva sintomática.

**Material y métodos:** Desde noviembre de 2011 a octubre de 2017, se intervino un total de 28 pacientes. Se analizaron la evolución posoperatoria, clínica y ecocardiográfica al alta y al seguimiento.

**Resultados:** Edad promedio  $53,3 \pm 13,4$  años. La mortalidad perioperatoria (<30 días) fue del 0%. Un paciente falleció a los 90 días (3,5%). No se produjeron comunicaciones interventriculares, daño de la válvula aórtica ni se reemplazó la válvula mitral en ningún paciente. El 91% de ellos se encontraban con disnea en CF III-IV en el preoperatorio, los restantes tenían angina o síncope. En el seguimiento, el 92,8% estaban asintomáticos, 1 paciente en CF III y otro en CF II. El gradiente preoperatorio basal promedio fue de 53,5 mmHg y con valsalva 86,4 mmHg; los gradientes basal y con valsalva posoperatorios fueron 9,4 mmHg y 13,5 mmHg ( $p < 0,01$ ). Al seguimiento, los gradientes en reposo y con valsalva fueron aún más bajos, 8,3 mmHg y 10,7 mmHg, respectivamente ( $p$ : NS). Nueve pacientes (32%) presentaban insuficiencia mitral moderada a grave previa por movimiento anterior sistólico o patología intrínseca mitral. Se detectó solo un paciente con insuficiencia mitral moderada asintomática en el seguimiento (3,5%). La mediana de seguimiento fue de 400 días, Pc 25-75 de 695 días (mínimo de 30 días y el máximo de 1868 días).

**Conclusión:** Con la miectomía septal ampliada se obtiene una mejoría hemodinámica y clínica de los pacientes sintomáticos, con bajo número de complicaciones posoperatorias. Esto tiene como resultado una mejor calidad de vida.

**Palabras Clave:** Cardiomiopatía Hipertrófica - Tabiques Cardíacos/cirugía -Tabiques Cardíacos/diagnóstico por imágenes. Procedimientos Quirúrgicos Cardíacos/métodos

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## INTRODUCTION

Obstructive hypertrophic cardiomyopathy (OHCM) is defined by the presence of increased left ventricular wall thickness that cannot be explained solely by abnormal loading conditions. (1-4) It is the most common genetic heart disease, and the leading cause of sudden death in young people, (5, 6) with a prevalence of 1 per 500 people in the general population.

Almost 60 years have passed since the first description of hypertrophic cardiomyopathy, based on invasive hemodynamic parameters by Brock in 1957 and on autopsies by Teare in 1958. (7-9) It is currently known that left ventricular outflow tract obstruction (LVOT) is present in approximately 70% of patients with resting or provoked hypertrophic cardiomyopathy. (10) This obstruction can generate symptoms by different mechanisms: it may limit cardiac output, producing symptoms of exertion such as dyspnea or pre-syncope, it can generate an increase in left ventricular end-diastolic pressure inducing ischemia, it can affect ventricular relaxation and diastolic filling and finally, mitral regurgitation (MR) due to systolic anterior motion (SAM) associated with the obstruction can produce increased left atrial pressure, dyspnea and atrial fibrillation (AF). (11, 12)

The primary endpoint of treatment is to improve symptoms, particularly those determined by LVOT dynamic obstruction. The first line of treatment is pharmacological, but around 25% of patients remain symptomatic. In these cases, surgical myectomy is the treatment of choice. (13) The usual indication for myectomy includes patients with severe LVOT obstruction with resting gradients  $>30$  mmHg. (14) However, indications have now been extended to include symptomatic patients with low resting gradients and latent obstruction. (15)

In our country, surgical treatment is limited to few centers, with unknown results. Therefore, the aim of this study was to evaluate the clinical and echocardiographic outcome of a population undergoing extended septal myectomy (ESM) for symptomatic OHCM, refractory to optimal medical treatment

## METHODS

Among 550 patients with hypertrophic cardiomyopathy monitored at the institution, we identified those undergoing invasive treatment by ESM. From November 2011 to October 2017, a total of 28 patients with OHCM, all refractory to optimal pharmacological treatment, underwent surgery. The treatment strategy and the clinical and echocardiographic assessment were carried out by members of the Cardiomyopathy Center, integrated by clinical cardiologists, interventional cardiologists, electrophysiologists, surgeons, and cardiac failure and imaging study specialists of our Institution. The postoperative (PO) clinical and echocardiographic outcomes were analyzed at discharge and at mid-term follow-up. Median follow-up was 400 days (25-75 IQR: 695 days (minimum 30 days and maximum 1,868 days).

Diagnosis and echocardiographic assessment was based on the echocardiogram of a non-dilated left ventricle with enhanced wall thickness ( $>15$  mm), with no other cardiac

or systemic cause responsible for a similar hypertrophy. End-diastolic wall thickness was considered as maximum thickness. Continuous-wave Doppler ultrasound was used to estimate peak gradient in the LVOT and obstruction was defined as the presence of gradient  $\geq 30$  mmHg at rest, with maneuvers or exercise.

## Surgical procedure

After induction of general anesthesia, a transesophageal echocardiogram (TEE) was performed to evaluate mitral valve morphology and its primary pathology, as well as to project the extension of myectomy. Maximum septal thickness was measured in several views, as well as maximum distance from the aortic valve to the site of maximum hypertrophy, SAM location and the extension towards the hypertrophy mid-ventricular and apical segments.

Following onset of cardiopulmonary bypass (CPB), aortotomy was performed exposing the basal septum. Then, two parallel incisions were done below the nadir at 8-10 mm of the right coronary leaflet, extending it to the base of the papillary muscles. Resection was completed towards the apex and continued leftward up to the anterior mitral valve leaflet and rightward up to the postero-medial commissure.

The mitral valve apparatus was explored, excising trabeculae, abnormal tendinous cords and papillary muscles that might provoke or favor the obstruction. In case of redundant anterior mitral leaflet, plication in its body was achieved with separate sutures.

Patients with paroxysmal or permanent AF underwent pulmonary vein bipolar ablation and left atrial appendage excision (Maze), and patients with coronary heart disease underwent concomitant coronary artery bypass grafting.

The TEE was repeated at the end of the procedure at the time of CPB weaning to assess residual gradients at rest and with provocative maneuvers. Systolic anterior motion, residual MR and presence of potential complications, as aortic regurgitation or ventricular septal defect (VSD), were also evaluated. In case there were still elevated gradients or SAM, CPB was reestablished to extend the myectomy or perform plication of the anterior mitral leaflet (Figure 1).

## Statistical Analysis

Patients' characteristics were expressed as mean  $\pm$  standard deviation, median and interquartile range (IQR) or prevalence (percentage), as appropriate. Differences between groups were analyzed with Student's *t* test for independent samples or with the Mann-Whitney U test for continuous variables, and the chi square test was used for categorical variables. A value of  $p < 0.05$  was considered statistically significant. IBM™ SPSS™ Statistics (version 21) software package was used to perform the analyses.

## Ethical considerations

The patients signed an informed consent for participation in the study that was carried out in compliance with the national personal data protection law 25.326.

The study was conducted according to national ethical standards (CABA Law 3301), the national law involving research in human subjects and the Declaration of Helsinki, and was approved by the institutional Research and Ethics Committee.

## RESULTS

Table 1 shows baseline characteristics of the study population. Mean age was  $53.3 \pm 13.4$  years and 15 pa-

tients were men (54%). Two patients (7.1%) had previous alcohol septal ablation. The average time from diagnosis to surgery was 8.13 years.

The predominant symptoms were angina in 25.9% of cases, dyspnea in 92.5% and syncope in 18.5%, with some patients suffering from more than one symptom. All patients were treated with beta blockers at maximum tolerated doses and 7 patients received concomitant calcium blockers. Eight patients had preoperative AF (29.6%) and in 7 cases (26.9%) the Maze procedure was performed.

Nine patients (32%) had prior moderate or severe MR, in two of them due to intrinsic mitral valve disease (prolapse, indentation) and in the rest due to secondary SAM for redundant anterior valve, anomalous tendinous cords or anterior implant of the papillary muscles. In the first patients, mitral valve repair was performed with correction of the valve pathology by left auriculectomy and the remaining patients underwent plication of the mitral anterior leaflet in its body or free edge, excision of abnormal tendinous cords or Alfieri stitch through the aortotomy. Five patients with coronary heart disease (17.8%), underwent coronary artery bypass grafting.

Two patients had implantable cardioverter defibrillator (ICD) for primary prevention implanted during their previous follow-up. Perioperative mortality (<30 days) was 0%. A patient who had perioperative stroke died 90 days after the procedure following multiple complications in a rehabilitation center, without achieving discharge after surgery (3.5%).

Complications in addition to the aforementioned stroke included an ischemic stroke with expressive

aphasia, with ad integrum restitution 30 days after surgery.

Four patients (14.2%) required permanent pacemaker implantation due to complete atrioventricular block in the immediate PO period and one of them at follow-up, due to repetitive syncope. Two patients (7.1%) received an ICD for primary prevention in the PO period and one at follow-up, without evidence of ventricular arrhythmias or appropriate shocks. These patients had a history of sudden death in the family.

Two patients presented PO AF (7.1%). This occurred in one of the patients who received surgical ablation, and in another it reversed with electrical cardioversion on PO day 5. In 12-lead Holter monitoring, only the patient with prior and PO AF continues fibrillated. No other patient with Maze procedure presented AF during follow-up. (Table 2)

There was no VSD, aortic valve damage or mitral valve replacement in any patient.

More than 90% of the patients presented with preoperative FC III-IV dyspnea. In the average follow-up of 572 days, 92.8% were asymptomatic, (1 patient in FC III and another in FC II).

The mid-term follow-up comprised 43.96 patients/year (range 1-56 months, mean of 17 months).

#### ECHOCARDIOGRAPHIC: Gradients

The average baseline preoperative gradient was 53.5 mmHg (range 16-104 mmHg) and the provoked gradient was 86.4 mmHg (range 44-186 mmHg). It is worth mentioning that only one patient presented gradient <50 mmHg with maneuvers, but also had moderate to severe MR secondary to SAM during exertion and recurrent paroxysmal AF with decompensation. Baseline and provoked PO gradients were 9.4 mmHg and 13.5 mmHg (p<0.01). At follow-up, resting and provoked gradients were even lower, 8.3 mmHg and 10.7 mmHg, respectively. (p: NS) (Figure 2 A and B) (Table 3).

#### Septal thickness and mitral regurgitation

Septal measurements varied between 16 and 34 mm (mean 21.9±4.5 mm) in the preoperative period. In the PO period, these were 13.2±3 mm (p<0.001). (Figure 2 C).

**Table 1.** Baseline population characteristics

Age (mean and standard deviation)	53.3±13.4
Age (range)	26 - 73
Men	15 (54%)
Family history of HCM	5 (17.8%)
Previous medication	
Beta blockers	28 (100%)
Calcium blockers	7 (25%)
ACEI	4 (14.2%)
Diuretics	2 (7.1%)
Amiodarone	3 (10.7%)
Oral anticoagulation	7 (25%)
Previous alcohol septal ablation	2 (7.1%)
Time since diagnosis	8.13 years
Angina	7 (25%)
Dyspnea	25 (92.5%)
Syncope	5 (18.5%)
Previous AF	8 (28.5%)
Coronary heart disease	5 (17.8%)
Moderate/severe mitral regurgitation	9 (32.1%)

HCM: Hypertrophic cardiomyopathy. ACEI: Angiotensin converting enzyme inhibitors. AF: Atrial fibrillation

**Table 2.** Operative/Postoperative data

Clamping time (mean±SD)	87.7±29.7
CPB time (mean±SD)	110.8±36.8
Maze procedure (n, %)	7 (25%)
Mitral valve plication	7 (25%)
Permanent pacemaker (n, %)	4 (14.2%)
Hospital stay (days, mean±SD)	5.4±2.67
Mortality at 30 days	0
Mortality at follow-up	1 (3.5%)

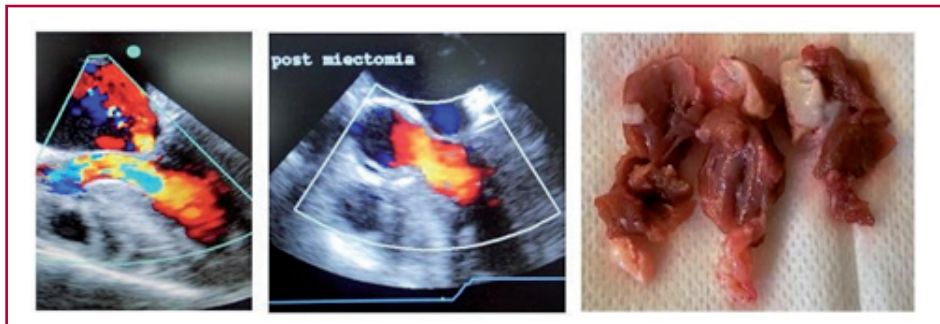
CPB: Cardiopulmonary bypass

Color Doppler studies showed moderate to severe MR in 32% of patients in the preoperative period. Moderate asymptomatic MR was detected in one patient at follow-up (3.5%), without severe regurgitation in any of them. Neither was moderate or severe aortic regurgitation observed at follow-up.

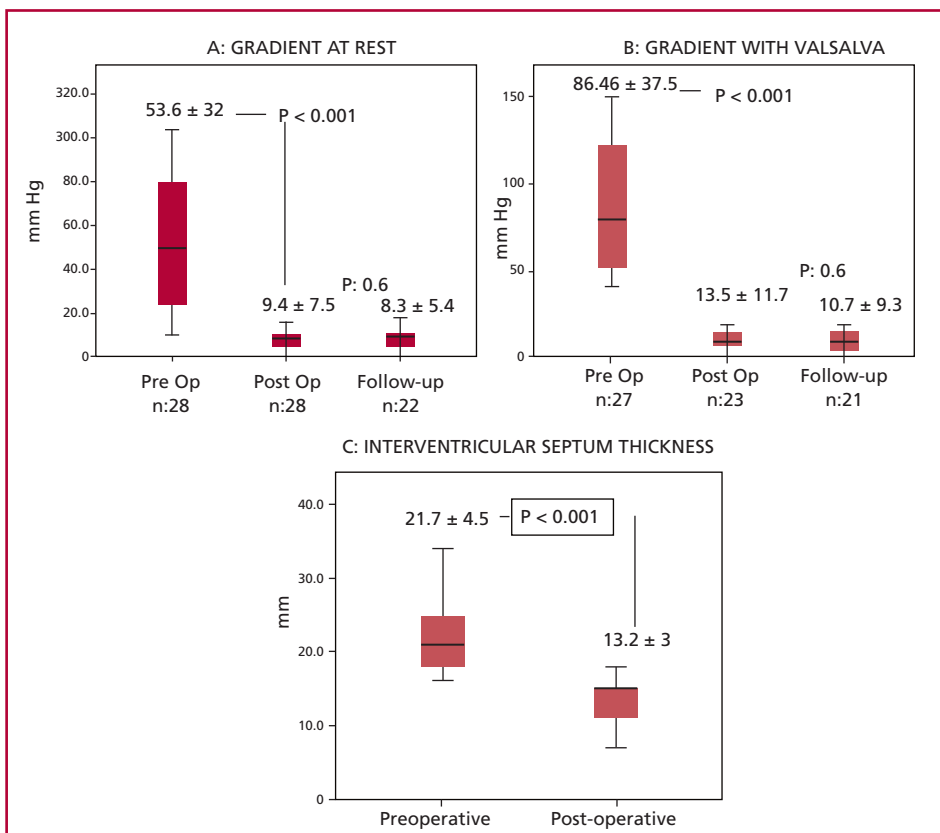
**DISCUSSION**

Consensuses and guidelines indicate that septal my-

ectomy is the treatment of choice for patients with symptomatic OHCM, refractory to medical treatment. (2-4) Decrease or elimination of LVOT gradients are obtained not only by the increase in its size as a result of ESM, but also by the interruption of the physiopathological events that cause the outflow tract gradients. The main event is SAM. Generally, the elimination of LVOT gradients by ESM results in the correction of the MR caused by SAM, and any residual



**Fig. 1.** Pre and post myectomy (A y B). Enlarged septal myectomy, surgical piece (C)



**Fig. 2.** Evolution of gradients and wall thickness

	Preoperative	Postoperative	Follow-up	p
Basal septum	21.7±4.5 mm	13.2±3 mm	-	<0.01
Gradient at rest	53.6±32 mmHg	9.4±7.5 mmHg	8.3±5.4 mmHg	<0.01
Gradient with Valsalva	86.4±37.5 mmHg	13.5±11.7 mmHg	10.7±9.3 mmHg	<0.01
Moderate/severe mitral regurgitation	9 (32%)	0	1	

**Table 3.** Doppler echocardiography



regurgitation secondary to chordal rupture, prolapse or annular dilatation may be corrected by valve repair and annuloplasty.

This initial experience report is part of a group of patients (approximately 5% of the total) followed up at the Institution's Center of Cardiomyopathies integrated by different specialists, who after discussing each case in particular, referred them for surgery. Among the 28 patients undergoing surgery since 2011, when the surgical program for OHCM was initiated, 19 were operated on in the last 3 years.

The choice of a surgical treatment was based on the fact that they were patients without significant comorbidities. It should be noted that our center also has the possibility of treatment through alcohol septal ablation, which is generally reserved for older patients with comorbidities or who refuse surgery. The concomitant presence of mitral valve or subvalvular apparatus anomalies and of atrial fibrillation, also favored the indication of surgery over alcohol ablation.

Morrow's original myectomy has been replaced by an expanded resection of the interventricular septum that has improved surgical results and is being used by more experienced surgical groups with better outcome.

Extended septal myectomy with mitral correction when necessary was associated with significant improvement of the clinical and hemodynamic characteristics of this initial series of patients, both in the immediate PO period as in mid-term follow-up. The LVOT gradients at rest and with Valsalva maneuver were significantly reduced in the immediate PO period and remain low at follow-up.

Functional class improved significantly and was maintained at follow-up. These data coincide with those of the most experienced centers in the world. (16, 17)

The most commonly described complications with myectomy are VSD and aortic regurgitation. Iatrogenic VSD occurs in less than 1% of patients and is more frequent when the septum does not exceed 16 mm in thickness. (13) Aortic or mitral valve injury is very rare when surgery is performed by an expert surgeon. (13) In our patients, VSD or aortic regurgitation were not present in the PO phase or at follow-up.

The need for a permanent pacemaker due to complete AV block is another usual complication. The figures reported in the literature involve 2% of the patients and it is more frequent in those with previous complete right bundle branch block and in patients with previous alcohol septal ablation, in whom the frequency may reach 20%. (18, 19) In our series, permanent pacemaker implantation for AV block was 14%. Among these four patients one presented with previous alcohol septal ablation with residual right bundle branch block, another had a history of high-grade AV block, and in another right and left Maze procedure was performed. We think that this figure is related to the previous history of alcohol septal ablation and

right bundle branch block and with the performance of complete right and left Maze procedure, with secondary AV block. In a recent meta-analysis, complete Maze procedure had an OR of 2.6 (95% CI: 1.09-6.20,  $p=0.031$ ) for the need of permanent pacemaker. (20) After these first cases, we limited the Maze procedure to pulmonary veins and to the left atrium, so that in the last 15 patients, only 1 required permanent pacemaker.

Perioperative mortality reported in different series varies between 0.5 and 1%. (21-24) Even centers without previous experience in this surgery have obtained encouraging results. (25, 26) In our experience, one patient died on PO day 90 due to multiple complications secondary to perioperative stroke.

Two patients presented perioperative stroke. Both patients required more than one admission in CPB to correct the pathology with consequent aortic re-clamping, which increases the risk of this complication. In the patient with stroke leading to death, there was tear of the ascending aorta, with sustained hypotension. We understand that the low number of patients magnifies the rate of this event expressed in terms of percentage, taking into account that international publications report figures of around 1% (23)

Plication of the mitral body or free edge has been described for excessively redundant mitral valve, a technique performed in 25% of our patients. This procedure eliminates the presence of residual SAM favored by previous implant of the papillary muscles and because the anterior mitral leaflet is redundant and contacts the septum despite correct myectomy. (12, 27) In addition, there is a group of patients in whom the septum is not severely hypertrophic, but the size of the anterior leaflet, the abnormal implant of tendinous cords and bifid papillary muscles are associated with LVOT obstruction. (28, 29)

In this initial experience, we treated 4 patients with mild hypertrophic septum ( $\leq 17$  mm) but with highly redundant mitral valve, in whom septal myectomy, valve plication and 2nd order cord excision was performed with good results regarding gradient reduction and MR and with clinical improvement.

Atrial fibrillation which is described in up to 25% of patients with OHCM and is four times more common than in the general population (30), was treated by bipolar ablation performed during the same surgery. Procedural success was high and, more importantly, 85.7% of patients (6 of 7) maintained sinus rhythm at follow-up, which is significant in the presence of possible complications associated with AF. (16, 31-33) This result should be taken with caution taking into account the number of patients in the study.

At follow-up, the clinical, echocardiographic and hemodynamic results show persistence of the initial improvement in symptoms and gradient reduction. Many published articles have reported that gradient reduction and clinical improvement with surgery change the disease outcome and increase patients'

survival. In this way, in the long term, the mortality of patients with this pathology is equated with the mortality of the general population. (22, 34)

The guidelines for the treatment of this disease determine that surgical treatment should be performed in centers with experience and surgeons trained in this technique. However, as in any surgical technique, after a logical learning curve and low risk of morbidity and mortality, it can be applied in new centers, with an initial low number of patients; however, it is very important to discuss these patients in a multidisciplinary team, evaluating the best treatment for each particular case. (25, 26)

### Limitations

The main limitation of the study is that the results analyzed correspond to a cohort of selected patients treated with ESM, with mid-term follow-up.

### CONCLUSION

This initial experience shows that when patients are followed up and selected for the best treatment available by a specialized multidisciplinary team, encouraging results may be obtained with ESM, which leads to hemodynamic and clinical improvement of patients in the short-term and during follow-up, resulting in better quality of life.

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