Adaptación materno-fetal a un programa de ejercicio supervisado durante la gestación

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Confirmo que Dña. Irene Fernández Buhigas ha llevado a cabo, bajo mi supervisión, los estudios presentados en la Tesis: *Adaptación materno-fetal a un programa de ejercicio supervisado durante la gestación*.

He leído la Tesis y estoy de acuerdo en que se presente en el programa de Doctorado en Biotecnología, Medicina y Ciencias biosanitarias de la Universidad Francisco de Vitoria.

Profesora Belén Santacruz Martín

Madrid, 06 de mayo de 2023

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ÍNDICE

ABREVIATURAS

GI: Grupo Intervención

GC: Grupo Control

DM. Diabetes Mellitus

Kg: Kilogramos

m^2: Metros cuadrados

ºC: Grados Celsius

FE: Fracción de eyección

IP: Índice de pulsatilidad

AST: Aspartato aminotransferasa

ALT: Alanina aminotransferasa

OMS: Organización Mundial de la Salud

IMC: Índice de Masa Corporal

ACOG: Colegio Americano de Obstetricia y Ginecología

SOCOG: Sociedad Canadiense de Obstetricia y Ginecología

FCF: Frecuencia cardiaca fetal

SEGO: Sociedad Española de Ginecología y Obstetricia

DA: Ductus Arterioso

Au: Arteria Umbilical

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RESUMEN

Introducción:

El ejercicio regular moderado supervisado durante la gestación está recomendado debido a sus múltiples beneficios. Sin embargo, los datos sobre el mecanismo de adaptación materno-fetal al ejercicio físico son escasos.

Métodos:

Se trata de ensayo clínico controlado aleatorizado llevado a cabo en el Hospital Universitario de Torrejón, en Madrid, España (NCT 02756143). Entre noviembre 2014 y junio 2015, se aleatorizaron 124 participantes a un programa de ejercicio supervisado moderado durante la gestación (grupo intervención) *vs*. no realizarlo (grupo control). Se recogieron datos clínicos, obstétricos, ultrasonográficos y analíticos accesibles en cada una de las visitas obstétricas. Posteriormente se realizaron diferentes análisis de los datos para intentar valorar las diferencias entre los grupos del estudio y así poder conocer mejor el mecanismo de adaptación materno-fetal al ejercicio físico.

Resultados:

No se encontraron diferencias significativas entre los grupos de estudio ni en el peso materno a las 20, 28, 36 y 38 semanas de gestación, ni en la ganancia ponderal durante el embarazo valorado en semana 38. Sin embargo, la proporción de participantes con una pérdida de peso superior a 9 Kg a las 6 semanas postparto fue mayor en el grupo intervención que en el grupo control.

Por otro lado, la fracción de eyección cardiaca fetal en la semana 36 de gestación fue mayor en los fetos del grupo intervención en comparación con los del grupo control. El resto de los parámetros cardiacos fetales evaluados fueron similares entre grupos.

No se encontraron diferencias significativas en el flujo vascular materno ni fetal en ningún momento del embarazo, siendo la edad gestacional el único factor que los modificó de manera constante, tal y como se espera de manera fisiológica. Sin embargo, el índice de pulsatilidad normalizado en *z-score* de la arteria umbilical evolucionó de manera diferente entre los grupos de estudio, siendo ligeramente mayor en el grupo intervención en la semana 20 para disminuir de manera paulatina hasta el parto, llegando a niveles ligeramente menores que el grupo control. Por el contrario, el mismo parámetro en el grupo control es estable alrededor del cero durante todo el embarazo, tal y como se espera de manera fisiológica.

No se encontraron diferencias en los resultados de las analíticas sanguíneas: glucosa en ayunas a las 12 ni a las 36 semanas de gestación, prueba de tolerancia de 50g de glucosa a las 26 semanas, aspartato aminotransferasa y alanina aminotransferasa a las 12 ni a las 36 semanas, creatinina sérica y ácido úrico séricos a las 36 semanas de gestación. La tensión arterial materna también fue similar entre los grupos salvo a las 28 semanas de gestación, donde la tensión sistólica fue significativamente menor en el grupo control respecto al grupo intervención. No se encontraron diferencias en el peso de las placentas entre ambos grupos de estudio.

Conclusiones:

Un programa de ejercicio físico de intensidad moderada supervisado durante la gestación no se asocia con una reducción en la ganancia ponderal materna, ni deterioro en el flujo vascular o parámetros analíticos maternos, sin embargo, favorece la pérdida de peso postparto. A nivel fetal, no solo no deteriora el flujo vascular, sino que, probablemente, asocia un mejor patrón adaptativo en la arteria umbilical y una mejor fracción de eyección cardiaca al final del embarazo. Finalmente, el peso placentario no se ve afectado por el ejercicio físico.

Palabras clave: ejercicio, actividad física, embarazo, resultados, peso placentario, recién nacido, *ductus* arterioso, función cardiaca fetal, peso materno, tensión arterial, glucosa, enzimas hepáticas, ácido úrico, Doppler, bienestar fetal.

ABSTRACT

Introduction:

Regular moderate and supervised exercise during pregnancy is worldwide recommended due to its proven benefits. However, the evidence about feto-maternal adaptation to exercise is still scarce.

Methods:

This is a randomized controlled trial carried out at the Hospital Universitario de Torrejón, in Madrid, Spain (NCT 02756143). From November 2014 to June 2015, 124 individuals were randomly assigned to perform a moderate supervised exercise program during pregnancy (Intervention group) or not to perform it (control group). Clinical, obstetric, ultrasonographic and analytical data available from all obstetric visits were collected. Several analyses were performed in order to evaluate differences between the groups and to better understand the feto-maternal adaptation to exercise.

Results:

No differences were found between the groups in maternal weight at 20, 28, 36 and 38weeks' gestation or in weight gain at 38 weeks. However, the proportion of individuals with a weight loss superior to 9 kg at 6 weeks postpartum was higher in the intervention group compared with the control group.

On the other hand, the fetal ejection fraction at 36 weeks was higher in the exercise group compared with the control group. All other evaluated fetal cardiac function parameters were similar between both groups.

No significant differences in the fetal or maternal Doppler measurements were found at any of the different check-up time points studied. The only variable that consistently affected the Doppler standardized values was gestational age at the time of assessment. The evolution of the umbilical artery Pulsatility Index z-score during the pregnancy was different in the two study groups, with a higher z-score in the exercise group at 20 weeks and a subsequent decrease until delivery, while in the control group it remained stable around zero.

No differences were found at the analytical results: fasting glucose at 12 or 36 weeks, 50 grams glucose tolerance at 26 weeks, Aspartate aminotransferase and Alanine aminotransferase at 12 and at 36 weeks, and blood Creatinine and Uric acid concentrations at 36 weeks. Maternal blood pressure was similar between groups except at 28 weeks, where systolic blood pressure was significantly lower in the control group compared to the intervention group. No differences in the placental weight at birth were observed between the two study groups.

Conclusions:

A regular supervised moderate exercise program during pregnancy is not associated with a reduction in maternal weight gain, does not deteriorate the vascular or analytical parameters, but it increases the postpartum weight loss. At fetal level, not only does not deteriorate vascular parameters, but it also probably associates a better adaptative pattern at the umbilical artery and a better fetal ejection fraction at the end of the pregnancy. Finally, placental weight is not affected by moderate exercise during pregnancy in healthy pregnant women.

Key words: exercise, physical activity***,*** pregnancy, outcomes, placental weight, newborn, *ductus* arteriosus, fetal cardiac function, maternal weight, blood pressure, glucose, hepatic enzymes, uric acid, Doppler, fetal wellbeing.

INTRODUCCIÓN

Según la Organización Mundial de la Salud (OMS), la inactividad física causa directamente el 20-25% de los cánceres de mama y colon, el 25% de la diabetes mellitus (DM) tipo 2 y del 30% de las enfermedades isquémicas[1,2]. La obesidad y la patología que asocia (hipertensión arterial, enfermedades cardiovasculares, DM, depresión, etc.) se ha convertido en un grave problema de salud mundial. La actividad física ha demostrado ser un método eficaz para reducir el riesgo no solo de estas patologías[3,4]. Por todo lo anterior, en las últimas décadas, se ha planteado la práctica regular de ejercicio como la clave para mejorar la salud física y mental de la población general.

De manera similar, diversos estudios han relacionado la obesidad materna con malos resultados perinatales y con un aumento del riesgo de obesidad infantil[5–8]. Actualmente, según las recomendaciones de la OMS, la ganancia ponderal recomendada durante la gestación debe basarse en el índice de masa corporal (IMC) previo (tabla 1)[9]. Por otro lado, parece que el buen control de la ganancia ponderal durante la gestación podría beneficiar al neonato y a la madre[5,10–20].

Tabla 1. Ganancia de peso recomendada durante el embarazo según el IMC de inicio de la gestación[9]

Índice de Masa Corporal materno pregestacional	**Ganancia de peso recomendada(kg)**
Bajo peso: <18,5 Kg/m^2	12,5-18
Normo-peso: 18,5-24,9 Kg/m^2	11,5-16
Sobrepeso: 25-29,9 Kg/m^2	7-11,5
Obesidad: >30 Kg/m^2	5-9

Existen diversos estudios que ponen de manifiesto que aproximadamente la mitad de las gestantes tienen una ganancia ponderal por encima de la recomendada según su IMC, y sólo un tercio de ellas tiene una ganancia ponderal adecuada[6]. La ganancia ponderal excesiva se asocia con un peso fetal aumentado, lo que condiciona un aumento de complicaciones perinatales como son el riesgo de cesárea, de distocia de hombros o de hipoglucemia neonatal[21]. Por otro lado, tras el puerperio aumenta la prevalencia de obesidad al asociarse con una menor pérdida ponderal y, a largo plazo, una mayor incidencia de DM tipo 2 y de enfermedades cardiovasculares en la mujer[22–24].

En España, un tercio de la población entre 16-69 años no alcanza los niveles de actividad física mínima recomendada por la OMS[9], y este incumplimiento es incluso mayor en mujeres[25]. En la Encuesta Europea de Salud de 2014, un 42% de las mujeres de más de 15 años se declararon sedentarias[26]. Entre las mujeres embarazadas, la tasa de sedentarismo es similar a la encontrada en la población general[27–29]. Algunos estudios comparan la actividad física de las gestantes en cada trimestre, encontrando que el sedentarismo es mayor en las gestantes de tercer trimestre respecto a las del segundo[30], posiblemente debido al aumento de las molestias derivadas del peso de la gestación y de los cambios a nivel musculoesquelético que se producen, así como los cambios a nivel de capacidad pulmonar[31,32].

Con el fin de disminuir las tasas de sedentarismo y la consecuente obesidad, las diferentes sociedades han diseñado estrategias poblacionales. Por ejemplo, la OMS y el Ministerio Español de Sanidad han puesto en marcha diferentes iniciativas y guías clínicas para disminuir la obesidad mundial y sus patologías derivadas, haciendo especial hincapié en la realización de ejercicio físico[33–35]. Sin embargo, la población gestante constituye un grupo delicado a la hora de recomendar ejercicio para evitar la excesiva ganancia ponderal pues aparecen numerosas dudas: ¿es el ejercicio seguro para la gestación y para la gestante?, ¿qué efectos tiene sobre la gestante a corto y largo plazo?, ¿qué efectos tiene sobre el futuro infante a corto y largo plazo? ¿todos los ejercicios son iguales? Son muchos los estudios que actualmente están intentando dar respuesta a estas preguntas.

1. Riesgos asociados a la práctica de ejercicio físico durante el embarazo

A lo largo de la historia las mujeres han recibido gran variedad de consejos y recomendaciones acerca de la actividad física adecuada durante el embarazo y, en general, la recomendación tradicional para una mujer gestante ha sido el reposo(36). No obstante, desde mediados del siglo pasado y especialmente en los últimos 40 años, muchos trabajos han demostrado la inocuidad del ejercicio físico moderado durante el embarazo en relación a la salud materna y fetal; incluso una cantidad importante de investigaciones informan de una asociación positiva entre el ejercicio aeróbico y moderado con buenos resultados maternos, fetales y del recién nacido(37).

Sin embargo, aunque diferentes guías como el Colegio Americano de Obstetricia y Ginecología (ACOG)(38) o la guía de la Sociedad Canadiense de Obstetricia y Ginecología (SOCOG)(39) o la Guía de práctica clínica sobre la actividad física durante el embarazo de la facultad de INEF(35) recomiendan la práctica de ejercicio físico durante la gestación, no hay que olvidar que no está exenta de riesgos. Como en la mujer no gestante, las **lesiones musculares** son el riesgo más común, siendo más frecuentes en los casos de mujeres que no realizaban previamente ejercicio(40). Lo que no está bien establecido es si estas lesiones pueden provocar realmente algún riesgo a la evolución del embarazo. Posiblemente, en casos de **golpes de gran impacto**, se pueda correr riesgo de desprendimiento prematuro de placenta normo inserta o de traumatismo fetal, aunque ningún estudio lo ha demostrado(41).

El miedo más extendido suele ser el del posible aumento de **abortos** de primer trimestre. De hecho, tradicionalmente, las mujeres suelen esperar a pasar este periodo para iniciar o retomar la práctica de ejercicio. La revisión de la literatura actual al respecto pone de manifiesto que la realización de ejercicio de intensidad moderada no parece tener ningún tipo de efecto sobre el riesgo de aborto(32,42) aunque no está claro si la realización de ejercicio físico de alta intensidad durante el primer trimestre (ejercicio con una intensidad mayor del 90% de la frecuencia cardiaca materna máxima) puede llegar a afectar en este sentido a la gestación(38,43).

Otro de los miedos habituales suele ser el riesgo de **parto prematuro** por la posible estimulación de las contracciones antes de tiempo. Es cierto que el ejercicio de intensidad vigorosa se ha asociado con el aumento de parto prematuro(44), sin embargo, en estudios más recientes se ha demostrado que esto no ocurre cuando se realiza ejercicio de intensidad moderada(32,45,46).

Dado que al realizar ejercicio se aumentan las necesidades de oxigenación por parte de los grupos musculares implicados, parece sensato pensar que la perfusión uteroplacentaria podría verse comprometida y, por lo tanto, **el bienestar fetal**. Varios estudios han intentado valorar el bienestar fetal durante la gestación mediante el test de Apgar y el pH de cordón al nacimiento[47,48]. Sin embargo, estos parámetros dependen en gran medida del desarrollo del parto más que del desarrollo del embarazo. Los fetos expuestos a una disminución de la perfusión uteroplacentaria normalmente asocian cambios en el Doppler útero-placentario y fetal, que empeoran el resultado perinatal y el desarrollo neurológico a largo plazo de esos niños[49–52]. Por lo tanto, investigar los cambios en los parámetros Doppler en las gestaciones cuyas madres realizan ejercicio de manera regular puede ayudar a evaluar el verdadero bienestar fetal durante la gestación.

Durante la realización de ejercicio físico se han observado diferentes alteraciones en la **frecuencia cardiaca fetal (FCF)**. Se han detectado episodios de bradicardia fetal transitoria, especialmente en casos de ejercicios de mayor intensidad, que el feto parece compensar con un aumento de su FCF posterior[53–56] de manera transitoria. En caso de ejercicio de intensidad leve-moderada o no aparecen estos episodios de bradicardia, o son de menor intensidad, sin apenas repercusión fetal[54,57,58].Por otro lado, sí se ha observado mediante cardiotocografía, un aumento transitorio de la FCF basal durante la realización del ejercicio, lo que supondría un mecanismo de adaptación a una menor perfusión útero-placentaria[10,54,59]. La bradicardia se produciría por un mecanismo vagal fetal ante la hipoxia secundaria al ejercicio, cuando otros mecanismos de adaptación dejan de ser suficientes. De todas maneras, las alteraciones de la FCF parecen normalizarse poco después de cesar el ejercicio. La mayoría de los estudios coinciden en que todas las alteraciones encontradas son transitorias y que es poco probable que puedan comprometer el bienestar fetal en gestaciones de bajo riesgo obstétrico[56,60,61].

Varios ensayos aleatorizados han estudiado el efecto de la realización de ejercicio físico de manera crónica durante la gestación[62–65]. Sin embargo, únicamente tres estudios evalúan el efecto del ejercicio mediante Doppler uteroplacentario y fetal[65–67]. En dos de ellos no se encontró ningún tipo de diferencia entre los grupos de gestantes que realizaban ejercicio durante la gestación y las que permanecían sedentarias[65,66]. Sin embargo, en el tercero, se encontró que, al someter a las gestantes a un test de esfuerzo en el tercer trimestre, el grupo de gestantes que realizaban ejercicio presentó un Índice de Pulsatilidad (IP) de la Arteria Umbilical (Au) significativamente menor al de las gestantes del grupo control tras la realización del test[67]. En otros estudios en los que se ha evaluado la respuesta al ejercicio a través del Doppler fetal, han demostrado que las alteraciones del Doppler debidas a la diminución del flujo uteroplacentario son más frecuentes cuando el ejercicio es de muy alta intensidad[53,56,58]. En una revisión sistemática reciente, no se encontraron alteraciones en el Doppler materno fetal debidas a la realización de ejercicio de manera regular durante la gestación, en mujeres de bajo riesgo obstétrico, con lo que concluyeron que el ejercicio realizado de acuerdo a las recomendaciones actuales de manera regular durante la gestación era seguro para el feto y neonato[68]. Es importante resaltar que este metaanálisis incluía estudios muy heterogéneos, la mayoría no aleatorizados y con muestras muy escasas, con intervenciones muy diferentes entre sí y con resultados también muy dispares. Por todo ello, los autores recomendaban la realización de nuevos estudios aleatorizados con protocolos bien establecidos para poder clarificar esta cuestión.

Otro de los posibles problemas que nos podríamos plantear es si realizar ejercicio pudiera condicionar un **retraso del crecimiento fetal** dado que, al aumentar las necesidades metabólicas maternas y el consumo de glucosa, las necesidades fetales pudieran no ser cubiertas. Los estudios evaluando las diferencias en el peso fetal al nacimiento muestran resultados diversos, habiendo evidencia tanto de que el ejercicio disminuye el peso fetal al nacimiento[69–71], como de que lo aumenta[72], o no tenga ningún efecto[73,74]. En una revisión sistemática del 2015 que incluyó 5322 gestantes de 28 ensayos clínicos aleatorizados, se concluyó que la realización de ejercicio regular supervisado disminuía el riesgo de tener fetos grandes para la edad gestacional, sin aumentar los fetos con retraso del crecimiento[75]. Sin embargo, en otro meta-análisis del 2018 no se encontraron diferencias en el peso fetal[76].

Otra de las consecuencias que podría tener interés es el **efecto teratogénico** de la hipertermia en la gestación, ya que la fiebre (39ºC) o la exposición a altas temperaturas en las primeras semanas del embarazo se ha asociado con defectos del tubo neural[77,78]. Soultanakis et al, en 1996, demostraron que la temperatura corporal de gestantes sanas que realizaban un ejercicio moderado no se elevaba más de 1ºC y en ningún caso superaba los 38ºC, por lo que parece poco probable que la práctica de ejercicio moderado pueda elevar la temperatura corporal hasta límites teratogénicos[79]. Cabe destacar que durante la gestación la termorregulación corporal es más efectiva, seguramente secundario a una vasodilatación periférica y al aumento del volumen plasmático y de la capacidad ventilatoria por minuto[80]. Sin embargo, no podemos concluir lo mismo en otras prácticas de ejercicio físico de intensidad vigorosa como maratón o *Hot yoga*, donde el aumento de la temperatura corporal suele ser mayor y no se ha demostrado que estos mecanismos compensatorios sean suficientes. Se ha postulado que la realización de ejercicios de alta intensidad en el agua podría disminuir este riesgo[(81)].

2. Beneficios asociados a la práctica de ejercicio físico durante el embarazo

Se han descrito múltiples consecuencias beneficiosas que el ejercicio realizado de una manera regular y supervisada puede tener durante la gestación, tanto para la madre como para el neonato[41].

A **nivel físico**, cabe esperar que el ejercicio tenga los mismos beneficios que en la mujer no gestante, mejorando la fortaleza, la flexibilidad, la resistencia, la coordinación y la velocidad[65,82–84]. Parece prevenir las molestias musculoesqueléticas típicas de la gestación (dolor de espalda, dolor suprapúbico, etc.)[85–87]. Además, la realización de ejercicio durante la gestación ya sea en agua o aeróbico, mejora los niveles de calidad de vida percibida[88–92].

En relación con la **salud mental**, es sabido que la gestación es un momento de gran vulnerabilidad para la mujer, siendo más proclive a desarrollar cuadros de depresión o ansiedad. A su vez, estos cuadros se han relacionado con malos resultados obstétricos (retraso del crecimiento, parto pretérmino, etc.) y con alteraciones en el desarrollo del recién nacido, el niño y el adolescente[93–104]. Finalmente, el desarrollo de depresión postparto puede tener consecuencias potencialmente graves tanto para la madre como para el hijo (menor apego madre-hijo, estancias prolongadas en el hospital, etc.)[103]. Por otro lado y tal y como ocurre en la población general, la realización de ejercicio en el embarazo parece disminuir los niveles de estrés, ansiedad y depresión a la vez que mejora la calidad del sueño[105–108]. Además, disminuye el riesgo de depresión postparto[105].

Algunos estudios han demostrado que la práctica de ejercicio físico durante la gestación puede disminuir la **ganancia ponderal**[9], lo que ayudaría a evitar la obesidad materna y sus consecuencias[109,109–116]. Como ya se ha expuesto anteriormente, la ganancia ponderal materna excesiva se asocia con mayor peso al nacimiento, lo que a su vez aumenta el riesgo de obesidad infantil[117]. Por otro lado, hay estudios que proponen que el ejercicio podría disminuir el peso al nacimiento sin comprometer el bienestar fetal[118,119], aunque otros estudios no encuentran ninguna diferencia[73].

En una revisión sistemática del 2014, se analizaron 11 ensayos tipo cohortes y 4 estudios de casos y controles para evaluar la relación entre el ejercicio físico y la **hipertensión arterial** en el embarazo[120]. Este estudio encontró una reducción del riesgo de preeclampsia de un 20-35% y de hasta un 50% en aquellas que ya lo realizaban previamente.

3. Cambios en la fisiología materna asociados a la práctica de ejercicio físico durante el embarazo.

Cambios cardiovasculares en la gestante que realiza ejercicio físico

Diversos estudios han puesto de relieve las modificaciones cardiovasculares que se producen en las gestantes que se someten a un programa de ejercicio físico durante la gestación[121,122]. Así, por ejemplo, en el 2012, Perales et al., describieron que, en las gestantes que seguían un programa de ejercicio físico moderado supervisado, se apreciaba un menor tiempo de relajación isovolumétrica, un mayor tiempo de deceleración de la onda E, valores significativamente superiores de volumen sistólico y valores significativamente mayores de llenado temprano del ventrículo[123]. Estas modificaciones cardiovasculares estarían reflejando una adaptación positiva del sistema cardiovascular materno, lo que facilitaría el desarrollo del tercer trimestre de embarazo y, además, controlaría factores de riesgo cardiovasculares maternos. Por otro lado, se ha descrito una menor frecuencia cardiaca materna en las gestantes que realizan ejercicio durante el embarazo, así como menor tensión sistólica y diastólica[11,36,123]. Un estudio aleatorizado encontró que la tensión sistólica en reposo de las gestantes normotensas que realizaban ejercicio durante el embarazo era menor que las que no lo hacían[124]. Todos estos hallazgos estarían traduciendo una adaptación cardiovascular materna a la realización de un ejercicio físico crónico durante el embarazo.

Se sabe poco de cuál es la base fisiológica para la menor tensión arterial y las consecuentes adaptaciones cardiovasculares que se observan en la mujer gestante que realiza ejercicio, pero se postula que el ejercicio reduce el estrés oxidativo, mejorando la función endotelial y las respuestas inmune e inflamatoria[125,126]. Apoyando esta teoría, se ha demostrado que el ejercicio aumenta los niveles de citoquinas antinflamatorias y disminuye las proinflamatorias[125]. Además, aumenta las defensas antioxidantes como la superóxido dismutasa y la glutatión peroxidasa en el plasma, hígado y músculo, y estimula la presencia de un mayor número de mitocondrias a nivel muscular y la unión del hierro a la apotransferrina, lo que, en conjunto, conlleva un menor estrés oxidativo[125].

Cambios metabólicos al ejercicio físico durante la gestación

Para un buen desarrollo fetal y neonatal es necesario un buen aporte de nutrientes durante la vida intrauterina[127]. El ejercicio aumenta el consumo de glucosa por los músculos; las concentraciones de glucosa en gestantes disminuyen durante un corto periodo de tiempo mientras realizan ejercicio, siendo esta disminución más acusada en el tercer trimestre de gestación[128]. Al mismo tiempo que se produce el descenso en la concentración de glucosa sanguínea, parece que se elevan ligeramente los niveles de triglicéridos, también de manera transitoria[128]. Por otro lado, parece que la práctica de ejercicio físico regular en la gestación disminuye los niveles de glucosa del test de cribado de diabetes gestacional (Test O'Sullivan, tolerancia oral de 50g Glucosa) a las 24-28 semanas de gestación[129,130]. Barakat et al(131) y Deierlein et al[129] concluyeron que el ejercicio durante la gestación mejoraba los resultados del test de cribado de diabetes gestacional, aunque no parecía disminuir la incidencia de diabetes[132–134]. Sin embargo, sí que parecía tener un efecto positivo en el control glucémico cuando ya existía una diabetes gestacional establecida.

Desde el punto de vista hepático, se ha descrito que el ejercicio físico en la población general aumenta los niveles sanguíneos y la actividad de la enzima aspartato aminotransferasa (AST), pero no se ha descrito qué ocurre durante la gestación[135,136].

A nivel renal, no parece que exista ningún efecto del ejercicio en la gestación, aunque la excreción de urea nitrogenada por la orina sí que podría verse afectada por la realización de ejercicio en población general no gestante[128,137].

4. Efectos en el desarrollo fetal

A finales de los años 80, el epidemiólogo DJP Baker, plateó que existe un origen fetal de la enfermedad coronaria del adulto en los recién nacidos con bajo peso. Y en 1998, formuló su hipótesis, según la cual la nutrición durante el periodo intrauterino determina la susceptibilidad a enfermar en la edad adulta[138]. Este fenómeno es conocido hoy en día como ***programming* fetal**, refiriéndose al hecho de que un estímulo determinado, si se produce durante el desarrollo precoz, genera cambios permanentes que persisten a lo largo de la vida. Se basa en los **cambios epigenéticos** que se producen por el ambiente intrauterino, el estrés, la nutrición, etc. Todos estos estímulos producirán una modificación de la expresión de los genes, sin cambiar la secuencia básica del ADN, para conseguir, con un único genotipo, diferentes fenotipos que se pueda adaptar a las circunstancias ambientales intrauterinas y a las esperadas en la infancia. Esta plasticidad es una ventaja evolutiva y ha sido estudiado principalmente en fetos expuestos a un ambiente intrauterino desfavorable, como es la insuficiencia placentaria o la diabetes[19,49,50,139–142]; Así por ejemplo, en el caso de insuficiencia placentaria y la consecuente malnutrición, el feto responderá alterando la estructura y función de varios órganos para conseguir preservar el desarrollo neurológico y lograr sobrevivir. Esos cambios conllevarán alteraciones en el número de células, mutaciones celulares que pueden conllevar cambios estructurales en los órganos, así como alteraciones metabólicas, que llevarán al feto a desarrollar un fenotipo "ahorrador" al nacimiento, en la que guardará y aprovechará cada gramo de alimento que tome.

Efectos del ejercicio durante la gestación en el desarrollo antropométrico del niño

La pregunta a contestar sería si la práctica de ejercicio físico durante el embarazo puede modificar el fenotipo fetal. Se ha realizado diferentes estudios con el fin de contestar a esta pregunta.

Existen varios estudios que parecen evidenciar que la práctica de ejercicio físico durante el embarazo puede modular no solo el peso, sino también la composición corporal del recién nacido[143,144] y que en los recién nacidos de madres que han realizado algún tipo de actividad física durante la gestación, se observado una disminución de la grasa corporal al nacimiento[145].

Y también parece demostrado, que el sobrepeso y la obesidad maternas previas a la gestación, así como el exceso de ganancia de peso durante el embarazo, se asocia con un aumento de la adiposidad de los niños a los 6 años de vida(7). Cabría pues pensar que la realización de ejercicio durante la gestación puede actuar modificando la grasa corporal del recién nacido a largo plazo, pero los estudios al respecto son escasos y controvertidos. En los casos de gestantes obesas existe evidencia de que la práctica de ejercicio físico durante el embarazo puede disminuir el tejido graso de los niños a los 6 meses del nacimiento(146). Sin embargo, en 2018 se publicaron los datos de un ensayo clínico aleatorizado con resultados que contradecían lo anteriormente publicado; en este estudio dividía a las gestantes en dos grupos (grupo ejercicio y grupo control)(147). Se analizaron un total de 57 niños (33 del grupo ejercicio y 24 del grupo control) y se demostró que los niños nacidos de las madres del grupo intervención presentaban los 7 años de vida, una mayor adiposidad total, así como una mayor adiposidad abdominal y un porcentaje mayor de grasa ginoide, en comparación con los niños del grupo control. Los autores proponen que el hecho de hacer ejercicio durante la gestación, si previamente no se había realizado, podría tener ese efecto adverso en la infancia del recién nacido. Otro ensayo clínico similar, analizó 300 niños a los 5 años de vida, 156 del grupo intervención y 144 del grupo control, y no encontró diferencias significativas en el IMC ni en la proporción de obesidad a los 5 años de vida(148), aunque en este estudio no se analizó la distribución de la grasa corporal.

Existen varios estudios que parecen evidenciar que la práctica de ejercicio físico durante el embarazo puede modular no solo el peso, sino también la composición corporal del recién nacido(143,144) y que en los recién nacidos de madres que han realizado algún tipo de actividad física durante la gestación, se ha observado una disminución de la grasa corporal al nacimiento(145).

Cambios cardiovasculares fetales en mujeres que realizan ejercicio durante el embarazo

Como hemos explicado anteriormente, debido al *programming* fetal, en los fetos que están expuestos a un ambiente intrauterino desfavorable, se producen una serie de modificaciones cardiovasculares fetales (corazones más pequeños, aumento de la velocidad de maduración de las células cardiacas, disminución del número de células cardiacas y enlentecimiento del crecimiento cardiaco, disminución del flujo en la aorta que produce vasos más estrechos y alteraciones endoteliales…), que podrían condicionar la salud cardiovascular durante la infancia y la etapa adulta(19,49,50,139–141).

Se han detectado diferentes formas de adaptación fetal al estrés que supone la práctica del ejercicio físico por parte de la gestante. La **FCF basal** se ve transitoriamente **aumentada** durante la realización del ejercicio(10,59), lo que sería un mecanismo de adaptación a una menor perfusión útero-placentaria(54). En casos de ejercicio físico intenso se puede llegar a producir una **bradicardia transitoria** por un mecanismo vagal fetal ante la hipoxia secundaria(54–56), siendo la aparición de esta bradicardia más probable cuanto mayor sea la intensidad del ejercicio(53). Cuando la madre realiza ejercicio durante la gestación, parece que se produce un **aumento de la variabilidad y de la FCF** en los fetos, y parece mantenerse hasta el mes de vida(149,150). Estos cambios estarían traduciendo una mejor salud cardiaca y un mejor desarrollo del sistema nervioso autónomo. Pero todos los cambios cardiacos fetales observados parece que son transitorios y en la mayoría de los estudios se concluye que es poco probable que puedan comprometer el bienestar fetal(56,60,61).

Como hemos visto anteriormente, el corazón fetal es muy sensible a los factores ambientales, por lo que cabe postular que, el ejercicio físico realizado regularmente en la madre podría generar una remodelación cardiovascular fetal que influyera en su vida de como adulto.

5. Tipo de ejercicio físico recomendado durante la gestación.

Se han publicado diversas guías clínicas específicas sobre ejercicio físico y gestación, donde se expone qué tipo de ejercicios son recomendables durante la gestación[151].

La guía clínica canadiense[39] y la guía de la Sociedad Española de Ginecología y Obstetricia (SEGO)[152], ambas del año 2019, advierten de que la mujer gestante debe ser activa diariamente y recomiendan la realización por parte de las gestantes de, al menos, 150 minutos de ejercicio físico de intensidad moderada. En la guía de la SEGO[152] además se recomienda la realización de ejercicio al menos 3 veces por semana, de manera regular (no ocasional), preferentemente guiada por un profesional y que desarrolle la resistencia aeróbica, la fuerza muscular leve, el equilibrio y la coordinación motriz, la flexibilidad y el trabajo de suelo pélvico.

En 2020 la ACOG publicó su última guía sobre el ejercicio durante la gestación y el postparto[38]. En ella se recomienda a todas las mujeres embarazadas sanas que, durante la gestación y el postparto, realicen al menos 150 min por semana de ejercicio aeróbico de intensidad moderado (equivalente a andar rápido). Esta actividad debería realizarse durante todo el embarazo ajustándose según las indicaciones médicas. La guía también recoge que las mujeres habituadas a realizar un ejercicio de intensidad alta o vigorosa (como correr) o que son altamente activas pueden continuar realizando actividad física siempre que el embarazo transcurra con normalidad. Además, asume las mismas premisas que la guía canadiense[39] y de la SEGO[152], incluyendo también que se debe combinar ejercicio aeróbico, ejercicios de fuerza y de suelo pélvico.

Se entiende como ejercicio moderado aquel que consigue una frecuencia cardiaca máxima moderada (40-59% de la reserva de la frecuencia cardiaca) (Tabla 2). Para poder controlar la frecuencia cardiaca y monitorizar que no supere la frecuencia cardiaca máxima recomendada, la gestante debe portar un monitor de frecuencia cardiaca continua durante la realización del ejercicio. Otra manera de monitorizar que el ejercicio sea moderado es utilizar el Talk test, que consiste en valorar si la persona es capaz de mantener una conversación durante la realización del ejercicio[39].

Tabla 2. Rangos de frecuencia cardiaca para gestantes[39]

Edad materna	***Intensidad***	***Frecuencia cardiaca materna (latidos/minuto)***
< 29 años	Baja Maderada Alta	102-124 125-146 147-169
> o = 30 años	Baja Moderada Alta	101-120 121-141 142-162

En la guía publicada por la ACOG en el 2015, se daban indicaciones precisas sobre los ejercicios que eran adecuados iniciar o continuar durante la gestación y cuales se debían evitar (Tabla 3)[112]. Sin embargo, en la actualización del 2020[38], se limita a establecer que es recomendable la realización de ejercicios aeróbicos y de fuerza antes, durante y después del embarazo, evitando los deportes de contacto y el submarinismo. Además, propone que los deportes en agua podrían ser mejor tolerados por la gestante. Establece una serie de señales de alarma que deben hacer que la gestante cese la realización de ejercicio físico (el sangrado vaginal, el dolor abdominal, la aparición de contracciones dolorosas regulares, pérdida de líquido amniótico, disnea antes de la realización de ejercicio, sensación de mareo, dolor de cabeza, dolor en el pecho, debilidad muscular que afecte la estabilidad y dolor o hinchazón en la pantorrilla).

En la Guía de la SEGO[152], se establecen una serie de contraindicaciones absolutas y relativas para la realización de ejercicio durante la gestación (Tabla 4), que también están presentes en la guía Canadiense[39] y de la ACOG[38]. En estos casos, habrá que valorar riesgos y beneficios de manera individualizada con su obstetra o matrona.

Tabla 3. ACOG Committee Opinion No. 650: Ejercicio y actividad física durante la gestación y puerperio[112]

Actividades seguras para iniciar o continuar	*Actividades que evitar durante la gestación*
- Caminar - Nadar - Bailar - Bicicleta estática - Ejercicios aeróbicos de bajo impacto - Ejercicios de resistencia - Ejercicios de estiramiento - Yoga modificado (Las posiciones de yoga que producen una disminución del retorno venoso o una hipotensión deben ser evitados) - Pilates modificado - Running, Jogging, juegos de raqueta, entrenamientos de fuerza, … (tras consultar a su obstetra y con su supervisión, estos ejercicios puedes ser seguros durante la gestación en gestantes que los practicaban previamente)	- Deportes de contacto (Hockey, boxeo, futbol, baloncesto, …) - Actividades con alto riesgo de caída (Ski con bajadas, Ski acuático, Surf, ciclismo en campo a través, gimnasia deportiva, hípica, …) - Submarinismo - Paracaidismo - “Hot yoga” - “Hot Pilates”

Tabla 4. *Contraindicaciones absolutas y relativas para la realización de ejercicio durante la gestación*[152]

Contraindicaciones absolutas	***Contraindicaciones relativas***
- Rotura de membranas - Amenaza de parto prematuro - Sangrado vaginal de 2º o 3º trimestre. - Placenta previa después de las 26-28 Semanas de gestación - Pre-eclampsia - Incompetencia cervical - Retraso del crecimiento intrauterina en la gestación actual - Gestaciones múltiples de alto grado (triples, …) - Enfermedades cardiovasculares, respiratórias o sistémicas graves - Anemia severa sintomática	- Anemia - Enfermedades cardiorrespiratorias moderadas-leves (Arritmias, bronquitis crónica, …) - Diabetes tipo I con mal control - Obesidad mórbida extrema - Muy bajo peso materno (IMC<12) - Malnutrición - Desórdenes alimentarios - Historia previa de vida extremadamente sedentaria - Retraso del crecimiento en la gestación actual - Hipertensión mal controlada - Limitaciones ortopédicas - Enfermedad epiléptica con escaso control - Hipertiroidismo no controlado - Grandes fumadoras - Abortos de repetición - Historia previa de parto prematuro - Gestaciones gemelares tras las 28 Semanas de gestación - Enfermedades maternas significativas

En definitiva, a la luz de la evidencia actual, se puede decir que el ejercicio físico de intensidad moderada durante el embarazo es seguro tanto para la gestante como para el feto y que podría ser beneficioso para ambos, ya que parece mejorar la salud presente y futura de la madre y parece mejorar la salud futura del feto. Sin embargo, toda la evidencia sigue siendo escasa ya que es un campo de investigación novedoso, donde hay poca literatura concluyente, con estudios cuya metodología no siempre es de alta calidad y el número de gestantes incluidas suele ser escaso. Por esta razón son necesarios más estudios aleatorizados y de alta calidad para poder poner luz sobre los riesgos y beneficios, tanto maternos como fetales, del ejercicio durante la gestación.

OBJETIVOS

Hipótesis de partida

Un programa de ejercicio físico de intensidad moderada durante el embarazo produce mecanismos de adaptación tanto maternos como fetales.

Objetivo primario:

- Valorar si la realización de un programa de ejercicio físico supervisado durante la gestación puede prevenir la excesiva ganancia ponderal materna durante el embarazo.

Objetivos secundarios:

- Evaluar los cambios en la función cardiaca fetal producidos en el grupo de gestantes que realizan un programa de ejercicio físico supervisado durante la gestación.
- Evaluar los cambios longitudinales en el flujo vascular arterial materno y fetal, medido por ecografía-Doppler en el grupo de gestantes que realizan un programa de ejercicio físico supervisado durante la gestación.
- Valorar cambios fisiológicos maternos y fetales asociados a la realización de un programa de ejercicio físico supervisado durante la gestación.

MÉTODOS

La presente Tesis, es un compendio de cuatro publicaciones, basadas en los resultados de un ensayo clínico controlado aleatorizado, realizado en el Hospital Universitario de Torrejón, Madrid, España, registrado en ClinicalTrials.gov, con N.º de registro NCT 02756143. El estudio fue aprobado por el Comité de Ética del Hospital Universitario Severo Ochoa (CEIC Hospital Universitario Severo Ochoa) el 06/07/2013 (Madrid, Espain) y se realizó en concordancia con las guías de ética de la Declaración de Helsinki (modificado en 2008).

Desde noviembre 2014 a junio 2015 se ofreció participar en el ensayo a 840 mujeres durante el primer trimestre de embarazo, que llevaban a cabo su control gestacional en el Hospital Universitario de Torrejón. Finalmente 209 gestantes aceptaron participar. De ellas, 85 fueron excluidas por no cumplir algún criterio de inclusión, por lo que finalmente se incluyeron en el estudio 124 gestantes.

Se realizó una aleatorización simple con el programa *Epidat V.3.*, para dividir a las gestantes en dos grupos: Grupo Intervención (GI) y Grupo Control (GC). Para esto, se creó una lista computarizada de números al azar (N=200) a través de la opción de grupos balanceados (pero no iguales) del *Epidat*. Debido a la falta de financiación, no se alcanzó el número de tamaño muestral suficiente calculado para demostrar diferencias en relación a la ganancia de peso materna entre los dos grupos.

Tras la aleatorización se excluyeron tres gestantes pertenecientes al GC: una padeció un aborto tardío espontáneo a las 20 semanas de gestación, otra presentó títulos altos de anticuerpos anti-Kell, aumentando su riesgo gestacional, y una tercera recusó el consentimiento informado unos días después de haber sido aleatorizada.

Los *criterios de inclusión* fueron:

- Edad gestacional <16 semanas.
- No realización de ejercicio de forma regular durante más de 30 min, 3 veces por semana.
- Capaz de comunicarse en español.
- Ser mayor de 18 años.

Los <u>*criterios de exclusión*</u> fueron:

- No poder asistir a las clases del programa de ejercicio físico
- La aparición de complicaciones obstétricas que contraindicasen la realización de ejercicio físico durante la gestación, establecidas en la guía de la ACOG del 2015(112).

Por protocolo se requería una adherencia mínima al programa de intervención del 70%. Los coordinadores del ensayo llevaron de manera regular el control de calidad de la recogida de datos, así como verificaron la adherencia a los protocolos.

La figura 1 muestra el diagrama de flujo del Ensayo clínico Aleatorizado.

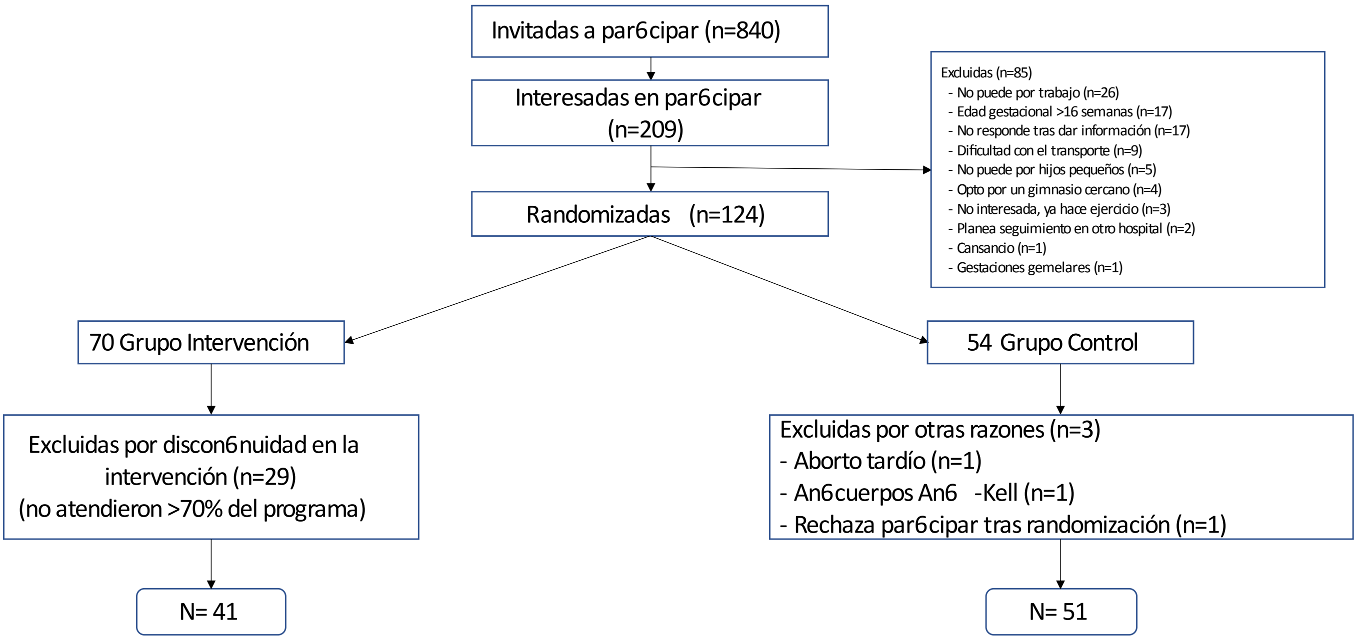

Figura 1. Diagrama de flujo

Con los datos obtenidos en el ensayo, se plantearon diferentes análisis, de los que se redactaron y publicaron los siguientes 4 artículos.

ARTÍCULOS PUBLICADOS

Estudio 1.- Does exercise during pregnancy impact on maternal weight gain and fetal cardiac function? A randomized controlled trial.

Brik M, **Fernández-Buhigas I**, Martin-Arias A, Vargas-Terrones M, Barakat R, Santacruz B.Ultrasound Obstet Gynecol. 2019 May;53(5):583-589.

1a- Corrigendum

Ultrasound Obstet Gynecol. 2022 Feb;59(2):279-280.

Estudio 2.- Fetal and maternal Doppler adaptation to maternal exercise during pregnancy: A randomized controlled trial.

Fernández-Buhigas I, Martin-Arias A, Vargas-Terrones M, Brik M, Rollé V, Barakat R, Muñoz Gonzalez MD, Refoyo I, Gil. MM, Santacruz B. J Matern Fetal Neonatal Med. 2023 Dec;36(1):2183759.

Estudio 3.- Maternal physiological changes at rest induced by exercise during pregnancy: A randomized controlled trial.

Fernández-Buhigas I, Brik M, Martin-Arias A, Vargas-Terrones M, Varillas D, Barakat R, Santacruz B. Physiol Behav. 2020 Jun 1;220:112863.

Estudio 4.- Does Exercise During Pregnancy Affect Placental Weight? A Randomized Clinical Trial.

Barakat R, Vargas M, Brik M, **Fernandez I**, Gil J, Coteron J, Santacruz B.

Eval Health Prof. 2018 Sep;41(3):400-414.

<u>Does exercise during pregnancy impact on maternal weight gain and fetal cardiac function? A randomized controlled trial</u>

Brik M, **Fernández-Buhigas I**, Martin-Arias A, Vargas-Terrones M, Barakat R, Santacruz B.Ultrasound Obstet Gynecol. 2019 May;53(5):583-589. doi: 10.1002/uog.20147. Epub 2019 Apr 2.

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Does exercise during pregnancy impact on maternal weight gain and fetal cardiac function? A randomized controlled trial

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KEYWORDS: ductus arteriosus; exercise; fetal cardiac function; maternal weight; physical activity

ABSTRACT

Objective *To evaluate the association between physical exercise during pregnancy and maternal gestational weight gain and fetal cardiac function.*

Methods *This was a randomized controlled trial of women with a singleton pregnancy managed from the first trimester at the Hospital de Torrejón, Madrid, between November 2014 and June 2015. Women were randomized to either follow a supervised physical conditioning program, consisting of a 60-min session 3 days per week for the duration of pregnancy, or not attend any exercise program (controls). The primary outcome was maternal weight gain during pregnancy. Secondary outcomes included fetal cardiac function parameters evaluated at 20, 28 and 36 weeks' gestation, Cesarean section, preterm delivery, induction of labor and birth weight. A sample size of 45 in each group was planned to detect differences in maternal weight gain of at least 1 kg, with a power of > 80% and* α *of 0.05.*

Results *During the study period, 120 women were randomized into the exercise (*n = 75*) and control (*n = 45*) groups. Following exclusions, the final cohort consisted of 42 women in the exercise group and 43 in the control group. Baseline characteristics (maternal age, prepregnancy body mass index, parity, conception by* in-vitro *fertilization, Caucasian ethnicity, physical exercise prior to pregnancy and smoker) were similar between the two groups. No differences were found between the groups in maternal weight at 20, 28, 36 and 38 weeks' gestation or in weight gain at 38 weeks. However, the proportion of women with weight loss ≥ 9 kg at 6 weeks postpartum was higher in the exercise compared with the control group (68.2%* vs *42.8%; relative risk 1.593;* $P = 0.02$*). The ductus arteriosus pulsatility index (DA-PI) at 20 weeks (2.43 ± 0.40* vs *2.26 ± 0.33,* $P < 0.05$*) and the ejection fraction (EF) at 36 weeks (0.85 ± 0.13* vs *0.81 ± 0.11,* $P < 0.05$*) were higher in the exercise compared with the control group. All other evaluated fetal cardiac function parameters were similar between the two groups.*

Conclusions *Performing exercise during pregnancy is not associated with a reduction in maternal weight gain but increases weight loss at 6 weeks postpartum. Physical exercise during pregnancy is associated with increased fetal DA-PI at 20 weeks and EF at 36 weeks, which could reflect adaptive mechanisms. Copyright © 2018 ISUOG. Published by John Wiley & Sons Ltd.*

INTRODUCTION

Maternal prepregnancy weight, body mass index (BMI), pattern of gestational weight gain and total gestational weight gain are factors that determine birth weight. In addition, birth weight and adiposity have a major impact on neonatal morbidity and mortality, and appear to affect early adult weight and long-term health[1–3].

Increased gestational weight gain has been associated with an increased risk of Cesarean section[4], pregnancy-related hypertension (gestational hypertension, pre-eclampsia)[5,6], gestational diabetes[7,8], neonatal adiposity[9] and childhood overweight or obesity[10].

Maternal exercise during pregnancy has been proved to be a preventive factor for developing hypertension during pregnancy, but there is controversy regarding its effect on reduction of excessive gestational weight gain. It has been suggested that it may control offspring size at birth while reducing comorbidities related to chronic disease risk[11].

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With respect to the fetus, exercise during pregnancy might increase fetal and infant heart-rate variability and determine the overall fetal health and the development of the fetal autonomic nervous system[12,13]. It is possible that maternal exercise during pregnancy may be associated with changes in fetal cardiac function parameters, but this has not yet been studied. Also, there is no study evaluating the association between gestational weight gain and fetal cardiac function parameters. This is relevant as the fetal heart could be sensitive to remodeling by environmental factors, as has been shown in growth-restricted fetuses affected by placental insufficiency[14].

The present study aimed to investigate whether following a supervised controlled exercise program throughout pregnancy prevents gestational weight gain that could be associated with a reduction in other pregnancy or birth complications. A secondary objective was to compare the incidence of Cesarean section, preterm delivery and induction of labor, as well as birth weight and fetal cardiac function parameters, between women who performed exercise during pregnancy and those who did not.

METHODS

Participants and trial design

This was a prospective randomized controlled trial of women with a singleton pregnancy who had pregnancy follow-up from the first trimester at the Hospital de Torrejón, Madrid, Spain. Inclusion criteria were: no obstetric or medical complications (based on the American College of Obstetricians and Gynecologists guidelines[15]); gestational age < 16 weeks; not exercising regularly during pregnancy, i.e. not performing more than 30 min of continuous exercise 3 days per week; and being able to communicate in Spanish. The exclusion criterion was non-availability to attend at least 70% of the exercise program of the study. Women having late miscarriage and high-risk pregnancy follow-up due to anti-Kell antibodies were also excluded.

Gestational age was estimated from menstrual history and confirmed by measurement of fetal crown–rump length at the first-trimester scan, which was performed routinely in all participating women.

Recruitment was performed from November 2014 to June 2015. Recruitment was stopped as soon as the required sample size was achieved. All women gave written informed consent to participate in the study. The study was approved by the local research ethics committee of the Hospital Universitario Severo Ochoa (19/07/2013) and was conducted in accordance with the ethical guidelines of the Declaration of Helsinki (modified in 2008). The study was registered at ClinicalTrials.gov (NCT 02756143). Trial coordinators undertook regularly quality-control checks of data handling and verification of adherence to protocols.

Randomization and masking

After written informed consent was obtained, women were allocated randomly to the control group or the exercise group in a 3:5 ratio. This ratio was selected because adherence to an exercise program during pregnancy is usually low so we expected a higher dropout rate in the intervention group. A computer-generated list of random numbers was used for allocation of participants to the two groups, generated using EPIDAT version 3.1 software (https://www.sergas.es/Saude-publica/Epidat-3-1-descargar-Epidat-3-1-(espanol)?idioma=es) with the option of balanced groups (similar but not equal size). One researcher (M.V.-T.) was responsible for the generation of the random allocation sequence, enrolment of participants and assignment of participants to interventions.

Intervention

The women in the exercise group undertook a supervised physical conditioning program consisting of three 60-min sessions per week for the whole duration of pregnancy (weeks 9–38). Each session included 10 min of warming up, 25 min of cardiovascular exercise, 10 min of strengthening exercises, 5 min of coordination and balance exercises, 5 min of pelvic floor exercises and 5 min of stretching and relaxation. Aerobic activity was prescribed at light to moderate intensity, aiming for 55–60% of maximum heart rate. All subjects wore a heart-rate monitor (Polar FT7; Polar, Madrid, Spain) during each training session to ensure that exercise intensity was mild to moderate.

Women in the control group were advised not to attend during pregnancy any supervised exercise program involving exercise for more than 30 min three times per week; however, they were not discouraged from exercising on their own. The women were questioned about their exercise practice at every clinical appointment.

Both groups were managed by the clinical team of the trial at a routine antenatal clinic. Obstetric ultrasound, including fetal echocardiography, was performed at 20, 28 and 36 weeks. The scans were performed by three researchers (I.F.-B., M.B. and A.M.-A.) blinded to the allocation group. All data were collected prospectively. Examinations were performed using a Voluson S8 (GE Medical Systems, Zipf, Austria) ultrasound system, in a standardized way, according to the guidelines of the International Society of Ultrasound in Obstetrics and Gynecology[16]. Women participating in the study received standard recommendations for nutrition and exercise[17].

The following fetal cardiac variables were measured by ultrasound: myocardial performance index (MPI), or Tei index, calculated as isovolumetric contraction time + isovolumetric relaxation time/ejection time[18]; tricuspid annulus plane systolic excursion (TAPSE); mitral annulus plane systolic excursion (MAPSE); tricuspid and mitral E/A ratios; and ejection fraction (EF).

MPI was assessed using a 2–10-MHz probe, in a four-chamber view, with the caliper placed at the basal area of the left ventricular wall (mitral annulus), interventricular septum and right ventricular wall (tricuspid annulus). The insonation angle was always < 30° to the ventricular wall. The angle was not corrected.

TAPSE and MAPSE were calculated in a four-chamber apical view, placing the caliper at the tricuspid annulus on the right ventricular wall (TAPSE) and at the mitral annulus on the left ventricular wall (MAPSE) with an angle of insonation of 0°[19].

Early (E) and late (A) peaks were measured in a four-chamber view, placing the pulsed Doppler gate just below the tips of the atrioventricular valves, and tricuspid and mitral E/A ratios were calculated[20].

EF was calculated according to the formula: EF = (end-diastolic volume − end-systolic volume)/end-diastolic volume. This measure was calculated in M-mode, tracing a line perpendicular to the interventricular septal wall on 2D ultrasound[21,22].

Outcome measures

Primary outcome was maternal weight change during and after pregnancy, evaluated at 20, 28, 36 and 38 weeks' gestation and 6 weeks postpartum. Gestational weight gain was calculated relative to prepregnancy weight. Postpartum weight loss was calculated relative to the last measurement of weight in the third trimester. Secondary outcomes were gestational and labor outcomes (Cesarean section, gestational age at delivery, preterm birth, defined as delivery < 37 weeks, induction of labor and perineal tear), perinatal outcome (birth weight, 5-min Apgar score < 6, arterial cord pH and admission to the neonatal unit) and fetal cardiac function parameters (MPI, TAPSE, MAPSE, mitral and tricuspid E/A ratios, aortic and pulmonary velocity, ductus arteriosus (DA) pulsatility index (PI), aortic isthmus PI and EF).

Statistical analysis

A conservative approach was followed for the sample-size calculation. We performed a power calculation for the primary outcome, maternal weight gain, assuming a bilateral alternative and considering a SD of 2.2 kg, based on the Institute of Medicine's recommendation for pregnancy weight gain of 11.5–16 kg in women with normal BMI[23]. Additionally, we wanted to detect

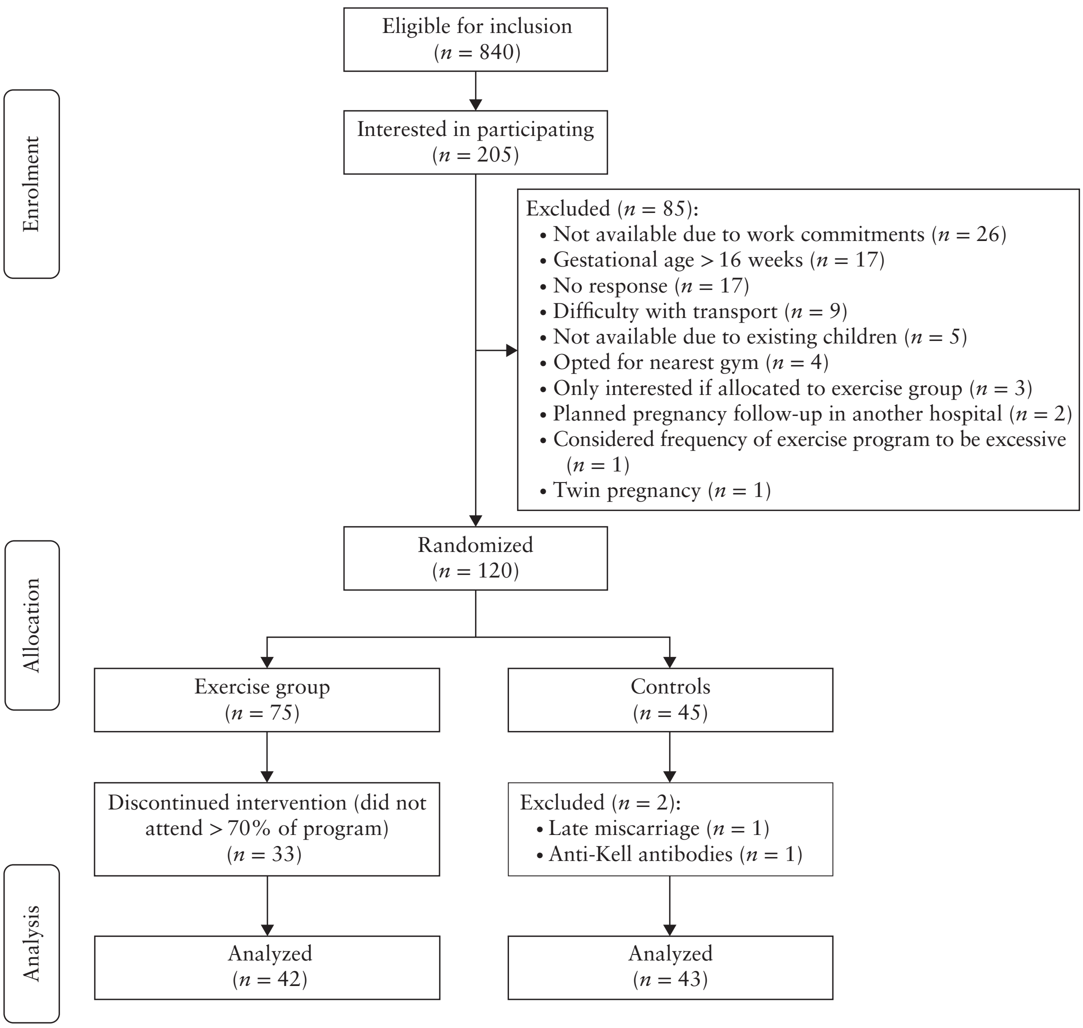

Figure 1 Flowchart showing enrolment in trial of women with singleton pregnancy and randomization to follow supervised controlled exercise program or not during pregnancy.

differences in maternal weight gain of at least 1 kg with a power of > 80% (> 0.8) and α of 0.05. Assuming a maximum loss to follow-up of 15%, we decided to recruit at least 45 participants to each study group.

SPSS statistical software version 23.0 (IBM Corp., Armonk, NY, USA) was used for all statistical analyses. Quantitative variables were expressed as mean with SD and qualitative variables as frequencies with percentages. Comparisons between groups were performed using the Mann–Whitney *U*-test. Univariate comparisons of dichotomous data were performed using Fisher's exact test. All tests were two-tailed, and *P*-values < 0.05 were considered statistically significant.

Table 1 Baseline characteristics of study participants randomized to follow supervised exercise program or not (controls) during pregnancy

Characteristic	*Exercise group* (n = 42)	*Controls* (n = 43)	P
Age (years)	33.4 ± 3.2	32.7 ± 4.4	0.466
Prepregnancy weight (kg)	63.5 ± 10	65.5 ± 15	0.944
Height (cm)	164.6 ± 6	164.2 ± 6	0.874
Prepregnancy BMI (kg/m^2)	23.4 ± 3.6	24.3 ± 5.3	0.762
Nulliparous	33 (78.6)	32 (74.4)	0.652
Conception by IVF	1 (2.4)	2 (4.7)	0.567
Caucasian ethnicity	41 (97.6)	41 (95.3)	0.567
Physical exercise before pregnancy*	15 (35.7)	9 (20.9)	0.129
Smoker	3 (7.1)	9 (20.9)	0.062

Data are expressed as mean ± SD or *n* (%). *Regular exercise, defined as ≥ 30 min continuous exercise 3 days/week. BMI, body mass index; IVF, *in-vitro* fertilization.

RESULTS

Between November 2014 and June 2015, 840 women were eligible for inclusion in the trial. Mean maternal age of the entire eligible cohort was 31.8 ± 5 years and mean prepregnancy BMI was 24.8 ± 4.4 kg/m^2; 54.9% of the women were nulliparous, 4.4% had conceived through *in-vitro* fertilization (IVF), 95.7% were of Caucasian ethnicity and 21.7% were smokers.

Of the total cohort of eligible women, 205 (24.4%) were interested in participating in the trial, and 41.5% of these were excluded mainly because of non-availability to attend the exercise program. Therefore, a total of 120 women were finally recruited and randomized to follow the supervised exercise program or not (Figure 1). Two women in the control group were excluded, one due to late miscarriage at 20 weeks and the other because of high-risk pregnancy (anti-Kell antibodies). In addition, 33 women from the exercise group did not attend more than 70% of the exercise program as required by the study, and were excluded from the final analysis. Therefore, the final study cohort consisted of 42 women in the exercise group and 43 in the control group. The two groups were similar with respect to maternal age, prepregnancy BMI, parity, conception by IVF, ethnicity, regular physical exercise before pregnancy and smoking (Table 1). Women in the control group reported (by telephone interviews) that they did not perform regular exercise during their pregnancy.

There was no difference in maternal weight at 20, 28, 36 and 38 weeks' gestation or in weight gain at 38 weeks between women who followed the exercise program and those who did not (Table 2). However, maternal weight

Table 2 Pregnancy and delivery outcomes of 85 women with singleton pregnancy according to whether they were randomized to follow supervised exercise program or not (controls) during pregnancy

Outcome	*Exercise group* (n = 42)	*Controls* (n = 43)	P	*Relative risk (95% CI)*
Maternal weight gain* at 38 weeks (kg)	11.4 ± 4.2	11.2 ± 6.4	0.82	
Maternal weight gain* at 38 weeks ≥ 16 kg	6 (14.3)	7 (16.3)	0.51	0.857 (0.262–2.801)
Maternal weight loss† at 6 weeks postpartum (kg)	9.7 ± 3	8.1 ± 3.5	0.01	
Maternal weight loss† at 6 weeks postpartum ≥ 9 kg	28/41 (68.3)	18/42 (42.9)	0.02	1.593 (1.060–2.393)
Maternal weight (kg) at:				
20 weeks' gestation	68.0 ± 10	67.8 ± 18	0.96	
28 weeks' gestation	67.8 ± 19	72.0 ± 19	0.66	
36 weeks' gestation	74.7 ± 11	74.3 ± 19	0.86	
38 weeks' gestation	75.5 ± 11	76.3 ± 15	0.86	
6–8 weeks postpartum	65.2 ± 11	68.9 ± 15	0.62	
Gestational age at delivery (days)	278 ± 9	277 ± 10	0.76	
Preterm delivery (< 37 weeks)	1 (2.4)	2 (4.7)	0.66	0.500 (0.044–25.732)
Cesarean section	3 (7.1)	6 (14.0)	0.86	0.474 (0.110–2.037)
Induction of labor	8 (19.0)	14 (32.6)	0.51	0.485 (0.178–1.323)
Perineal tear	29 (69.0)	25 (58.1)	0.70	1.606 (0.658–3.918)
Birth weight (g)	3161 ± 436	3201 ± 515	0.36	
Birth weight < 10th centile	7 (16.7)	8 (18.6)	0.19	0.825 (0.269–2.529)
5-min Apgar score < 6	0 (0)	0 (0)	—	
Arterial cord pH	7.28 ± 0.08	7.27 ± 0.07	0.79	
Admission to NNU	1 (2.4)	4 (9.3)	0.36	0.238 (0.025–2.222)

Data are expressed as mean ± SD or *n* (%). *Relative to pregregnancy weight. †Relative to last measurement of weight in third trimester. NNU, neonatal unit.

Table 3 Fetal cardiac function parameters at 20, 28 and 36 weeks' gestation, according to whether women were randomized to follow supervised exercise program or not (controls) during pregnancy

Parameter/ gestational age	*Exercise group (n = 42)*	*Controls (n = 43)*	P
MPI			
20 weeks	0.46 ± 0.11	0.47 ± 0.09	0.476
28 weeks	0.48 ± 0.11	0.50 ± 0.10	0.231
36 weeks	0.51 ± 0.14	0.53 ± 0.14	0.716
TAPSE (mm)			
20 weeks	0.43 ± 0.12	0.47 ± 0.12	0.376
28 weeks	0.58 ± 0.19	0.62 ± 0.17	0.249
36 weeks	0.60 ± 0.27	0.69 ± 0.20	0.162
MAPSE (mm)			
20 weeks	0.40 ± 0.17	0.39 ± 0.10	0.281
28 weeks	0.48 ± 0.19	0.50 ± 0.14	0.426
36 weeks	0.58 ± 0.20	0.60 ± 0.17	0.879
Tricuspid E/A ratio			
20 weeks	0.64 ± 0.70	0.63 ± 0.07	0.441
28 weeks	0.69 ± 0.11	0.69 ± 0.70	0.694
36 weeks	0.72 ± 0.10	0.70 ± 0.09	0.343
Mitral E/A ratio			
20 weeks	0.61 ± 0.78	0.58 ± 0.07	0.168
28 weeks	0.68 ± 0.09	0.68 ± 0.06	0.886
36 weeks	0.84 ± 0.76	0.69 ± 0.11	0.163
Aortic velocity (cm/s)			
20 weeks	63.58 ± 11.00	67.44 ± 10.00	0.190
28 weeks	78.21 ± 10.80	77.07 ± 13.40	0.495
36 weeks	81.82 ± 13.70	87.59 ± 12.10	0.168
Pulmonary artery velocity (cm/s)			
20 weeks	62.40 ± 10.00	63.19 ± 9.60	0.686
28 weeks	75.02 ± 16.70	73.58 ± 13.10	0.810
36 weeks	83.45 ± 16.15	83.54 ± 15.39	0.432
Ductus arteriosus PI			
20 weeks	2.43 ± 0.40	2.26 ± 0.33	0.049
28 weeks	2.34 ± 0.40	2.34 ± 0.28	0.623
36 weeks	2.50 ± 0.42	2.37 ± 0.29	0.116
Aortic arch PI			
20 weeks	2.57 ± 0.43	2.47 ± 0.32	0.109
28 weeks	2.50 ± 0.37	2.51 ± 0.32	0.663
36 weeks	2.57 ± 0.41	2.51 ± 0.33	0.699
Ejection fraction (%)			
20 weeks	0.86 ± 0.70	0.84 ± 0.09	0.412
28 weeks	0.88 ± 0.59	0.84 ± 0.10	0.093
36 weeks	0.87 ± 0.08	0.82 ± 0.10	0.033

Data are expressed as mean ± SD. E/A, E-wave/A-wave; MAPSE, mitral annular plane systolic excursion; MPI, myocardial performance index; PI, pulsatility index; TAPSE, tricuspid annular plane systolic excursion.

loss at 6 weeks postpartum was higher in the exercise group compared with the control group (9.7 ± 3 kg *vs* 8.1 ± 3.5 kg, $P = 0.01$), while the proportion of women with weight loss ≥ 9 kg at 6 weeks postpartum was higher in the exercise than in the control group (68.2% *vs* 42.8%; relative risk, 1.593 (95% CI, 1.060–2.393); $P = 0.02$).

Pregnancy and delivery outcomes were similar between the two groups in terms of incidence of Cesarean section, preterm birth < 37 weeks, induction of labor, perineal tear and birth weight (Table 2). When comparing birth weight adjusted for gestational age, there was no difference between the exercise and the control group in birth weight below the 10th centile (16.6% *vs* 18.6%, $P = 0.19$).

Fetal cardiac function parameters at 20, 28 and 36 weeks' gestation are presented in Table 3. MPI, TAPSE, MAPSE and tricuspid and mitral E/A ratio at 20, 28 and 36 weeks' gestation were similar between pregnancies that followed the supervised exercise program and those that did not. However, DA-PI at 20 weeks (2.43 ± 0.40 *vs* 2.26 ± 0.33, $P < 0.05$) and EF at 36 weeks (0.87 ± 0.08% *vs* 0.82 ± 0.10%, $P < 0.05$) were higher in the exercise group compared with the control group. No differences were found between the two groups in aortic velocity, pulmonary artery velocity and aortic arch PI at the gestational ages studied (20, 28 and 36 weeks).

DISCUSSION

Main findings

The findings of our study indicate that exercise during pregnancy does not reduce maternal weight gain, but increases maternal weight loss after delivery. In addition, exercise during pregnancy does not affect fetal cardiac function. The differences observed in DA-PI and EF between the exercise and control groups could reflect an adaptation in the DA blood flow, increasing the DA-PI at 20 weeks and leading to a better EF at 36 weeks of gestation in the exercise group.

Comparison with previous studies

Few systematic reviews have studied the relationship between physical activity and gestational weight gain or postpartum weight loss. A meta-analysis of physical activity and weight management in pregnant women suggested that physical activity may restrict gestational weight gain[24]. Similar findings were reported in two more studies, though the reduction in maternal weight gain was variable, with odds ratios ranging from 0.50 to 0.80[25,26]. It is not clear whether this reduction is higher in obese, overweight or normal-weight women. The present study includes mainly women with normal prepregnancy BMI, which could be the reason why our results are not concordant with previous studies.

Barakat *et al.* found no difference in maternal weight loss in the postpartum period between women who exercised and those who did not[27]. The present study showed significantly higher maternal weight loss after delivery in women exercising during pregnancy; the larger sample size could be an explanation for the statistically significant result.

Pathophysiological basis and insights

The DA is one of the most important vessels of the fetal circulation. In the normally developed fetus, 90% of the right ventricular stroke volume is shunted via the DA towards the descending aorta. DA-PI does not change with gestational age, ranging between 1.9 and 3 (mean, 2.46 ± 52)[28]. Under normal conditions, the DA has a high level of intrinsic tone during fetal life. The exact underlying mechanisms that cause premature constriction of the DA are still the subject of investigation[29,30]. Physiologically, the DA remains maximally dilated until term, actively sustained by regulatory control of prostaglandins and nitric oxide, which are produced within the ductal tissue[29].

Recently, a variety of substances have been identified as exerting vasoconstriction on the DA, as established for non-steroid anti-inflammatory drugs[31,32]. Echocardiographic diagnosis of progressive ductal constriction is further based upon increased systolic and diastolic peak velocities in the DA, resulting in a PI of less than 1.9[28].

The present study shows that exercise during pregnancy may induce a higher PI in the DA at 20 weeks and this effect could be preventive for early closure of the DA. This could be related to an interaction with the regulatory control of prostaglandins and nitric oxide, produced within the ductal tissue. It has been reported that acute exercise (as opposed to exercise training, i.e. low-intensity exercise) in pregnant women is associated with increased sympathoadrenal and neurohumoral activity[33]. We hypothesize that these biochemical changes may interfere with the control of prostaglandins and nitric oxide within the ductal tissue.

In the non-pregnant state, exercise improves oxygenation in the muscles and the skin but oxygen delivery to most viscera falls because of a decrease in blood flow. During pregnancy, the exercise effect on visceral flow persists but oxygen delivery to and utilization by the fetoplacental unit is maintained by several mechanisms that include maternal hemoconcentration and improved placenta–perfusion balance at the placental interface. Even though oxygen uptake is maintained, the fall in the placental bed blood flow shifts oxygen delivery to a lower point on the oxyhemoglobin dissociation curve. This lowers fetal partial pressure of oxygen which, in the human, initiates a sympathetic response that increases fetal heart rate[34]. However, experimental evidence indicates that tissue perfusion and oxygenation must be maintained at normal levels because no increased levels of erythropoietin in either cord blood or amniotic fluid have been shown[34].

The DA is widely patent in fetal life. The factors contributing to the maintenance of ductal patency in the fetus include exposure to low partial pressure of oxygen, prostaglandins and local nitric oxide production. Oxygen has been shown to be associated with constriction of the DA *in vitro* and *in vivo*[35].

Fetal EF in exercising pregnant women has not yet been investigated. This is the first study to show an increase in fetal EF at 36 weeks in women following an exercise program compared with controls.

The present randomized controlled trial is the first to study fetal cardiac function in relation to exercise during pregnancy. Functional echocardiography has been demonstrated to select high-risk populations and to be associated with outcome in several fetal conditions; however, it has not yet been incorporated into clinical practice[36]. It is well known that cardiovascular diseases in adulthood undergo a long subclinical phase over time, which may start in childhood or even in fetal life[37]. Fetal programming of adult cardiovascular diseases occurs when a stimulus or an insult in the *in-utero* environment during a sensitive period of cardiovascular development permanently alters cardiovascular structure and function.

Strengths and limitations

The main strength of this study is that it is the first randomized controlled trial to assess fetal cardiac function parameters in relation to the practice of a supervised exercise program during pregnancy.

We detected differences in the DA-PI and EF in both study groups, although the sample size was not calculated to investigate these parameters.

Limitations of the present study are the limited sample size and the size difference between the two groups, which can be explained by the simple randomization method used[38]. Moreover, the rate of nulliparous women in our cohort was higher compared with that in the general low-risk pregnant population followed in the Hospital de Torrejón (76.6% *vs* 54.9%) and this could represent selection bias. Finally, the study would have been enhanced if specialized nutritional counseling and follow-up, as well as a questionnaire to assess the physical activity performed in both groups during pregnancy, had been included in the study protocol.

Conclusions

The performance of moderate physical exercise throughout pregnancy increases weight loss after delivery and may have a beneficial association with fetal cardiovascular development; however, the long-term impact is still unknown. Large prospective studies are needed to elucidate the relationship between exercise during pregnancy and maternal weight and fetal cardiovascular function.

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Corrigendum

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Corrigendum

Brik M, Fernández-Buhigas I, Martin-Arias A, Vargas-Terrones M, Barakat R, Santacruz B. Does exercise during pregnancy impact on maternal weight gain and fetal cardiac function? A randomized controlled trial. *Ultrasound Obstet Gynecol* 2019; **53**: 583–589.

In this article, nine patients were inadvertently misclassified in the analysis. The correct number of patients in the exercise group is 41 and the correct number of patients in the control group is 51. The corrected Figure 1 and Tables 1–3 are appended below. In the entire eligible cohort, mean maternal age was 32.9 ± 4.1 years and mean prepregnancy body mass index was 23.4 ± 4.5 kg/m^2; 75.0% of women were nulliparous, 3.3% had conceived through *in-vitro* fertilization, 95.7% were of Caucasian ethnicity and 34.8% were smokers. Other information affected by the reclassification of women in the exercise and control groups is highlighted in Appendix S1.

Table 1 Baseline characteristics of study participants randomized to follow supervised exercise program or not (controls) during pregnancy

Characteristic	*Exercise group* (n = 41)	*Controls* (n = 51)	P
Age (years)	33.17 ± 3.19	32.63 ± 4.66	0.510
Prepregnancy weight (kg)	63.65 ± 10.90	66.10 ± 14.56	0.380
Height (cm)	164.68 ± 6.89	164.14 ± 5.84	0.682
Prepregnancy BMI (kg/m^2)	22.81 ± 3.54	23.80 ± 5.09	0.293
Nulliparous	31 (75.6)	38 (74.5)	0.904
Conception by IVF	1 (2.4)	2 (3.9)	0.611
Caucasian ethnicity	40 (97.6)	48 (94.1)	0.626
Physical exercise before pregnancy*	26 (63.4)	23 (45.1)	0.095
Smoker	10 (24.4)	22 (43.1)	0.061

Data are expressed as mean ± SD or *n* (%). *Regular exercise, defined as ≥ 30 min continuous exercise 3 days/week. BMI, body mass index; IVF, *in-vitro* fertilization.

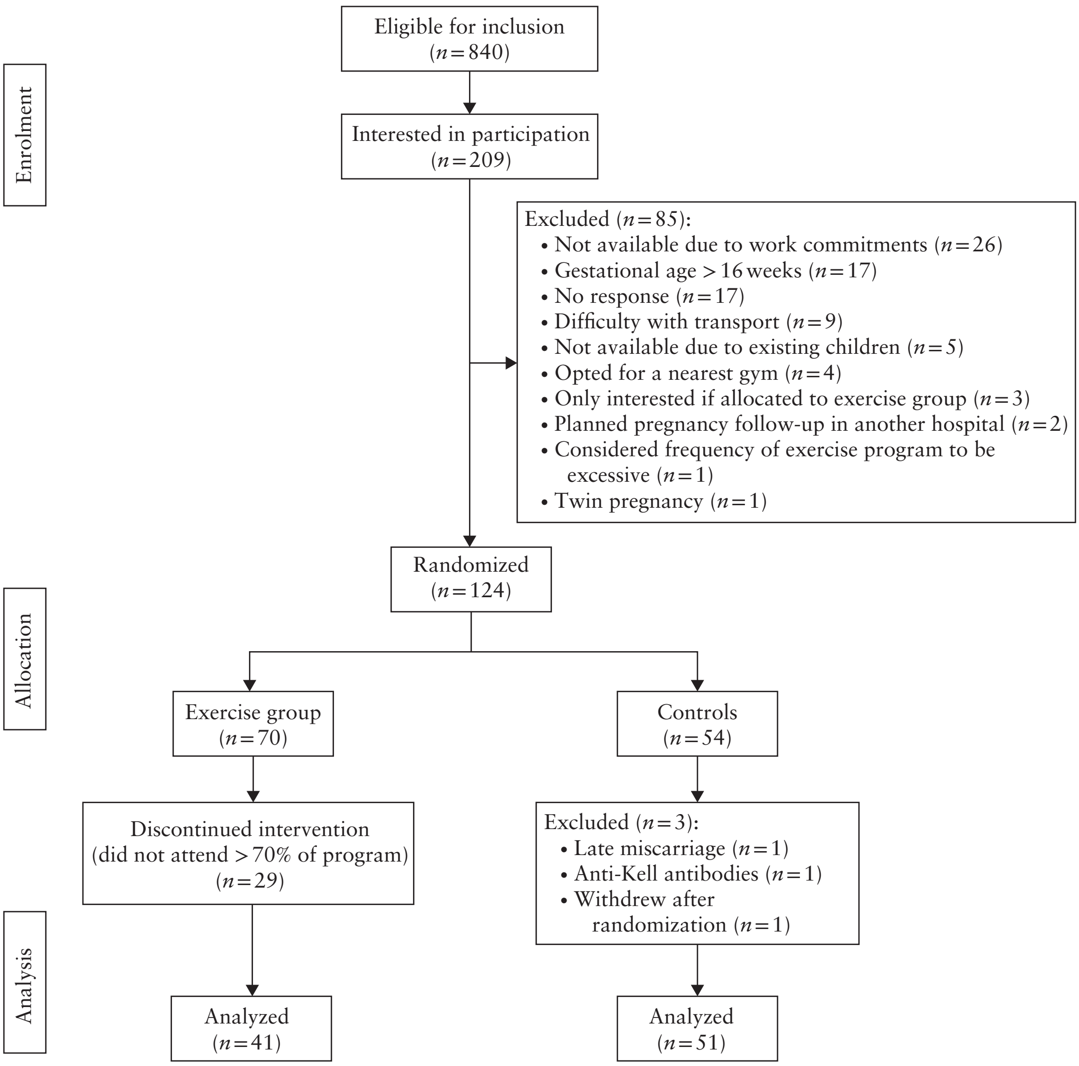

Figure 1 Flowchart showing enrolment in trial of women with singleton pregnancy and randomization to follow supervised controlled exercise program or not during pregnancy.

Table 2 Pregnancy and delivery outcomes of 85 women with singleton pregnancy according to whether they were randomized to follow supervised exercise program or not (controls) during pregnancy

Outcome	*Exercise group* (n = *41*)	*Controls* (n = *51*)	P	*Relative risk (95% CI)*
Maternal weight gain* at 38 weeks (kg)	13.2 ± 3.45	12.0 ± 6.25	0.574	
Maternal weight gain* at 38 weeks ≥ 16 kg	8 (19.5)	16 (31.4)	0.237	0.62 (0.29–1.31)
Maternal weight loss† at 6 weeks postpartum (kg)	9.63 ± 3.10	8.08 ± 5.00	0.033	
Maternal weight loss† at 6 weeks postpartum ≥ 9 kg	27 (65.9)	19/46 (41.3)	0.031	1.60 (1.06–2.40)
Maternal weight (kg) at:				
20 weeks' gestation	67.96 ± 10.66	70.11 ± 14.50	0.709	
28 weeks' gestation	71.46 ± 11.13	73.66 ± 14.70	0.727	
36 weeks' gestation	74.48 ± 11.54	76.85 ± 15.05	0.691	
38 weeks' gestation	75.15 ± 11.57	76.25 ± 15.47	0.916	
6–8 weeks postpartum	65.5 ± 11.3	67.4 ± 15.7	0.909	
Gestational age at delivery (days)	278.76 ± 9.45	276.08 ± 11.45	0.358	
Preterm delivery (< 37 weeks)	2 (4.9)	3 (5.9)	1	0.83 (0.15–4.73)
Cesarean section	4 (9.8)	7/50 (14.0)	0.748	0.69 (0.22–2.22)
Induction of labor	18 (43.9)	24/49 (49.0)	0.675	0.90 (0.57–1.40)
Perineal tear	28 (68.3)	30/49 (61.2)	0.515	1.12 (0.82–1.51)
Birth weight (g)	3160 ± 440	3160 ± 534	0.906	
Birth weight < 10th centile	13 (31.7)	13 (25.5)	0.642	1.24 (0.65–2.38)
5-min Apgar score < 6	0 (0)	1 (2.0)	1	
Arterial cord pH	7.29 ± 0.08	7.27 ± 0.07	0.317	
Admission to NNU	1 (2.4)	6 (11.8)	0.126	0.21 (0.03–1.65)

Data are expressed as mean ± SD, *n* (%) or *n*/*N* (%). *Relative to pregnancy weight. †Relative to last measurement of weight in third trimester. NNU, neonatal unit.

Table 3 Fetal cardiac function parameters at 20, 28 and 36 weeks' gestation, according to whether women were randomized to follow supervised exercise program or not (controls) during pregnancy

Parameter/ gestational age	*Exercise group* (n = *41*)	*Controls* (n = *51*)	P
MPI			
20 weeks	0.451 ± 0.104	0.475 ± 0.086	0.343
28 weeks	0.472 ± 0.115	0.499 ± 0.107	0.157
36 weeks	0.523 ± 0.146	0.532 ± 0.139	0.939
TAPSE (mm)			
20 weeks	0.453 ± 0.136	0.459 ± 0.107	0.975
28 weeks	0.584 ± 0.190	0.625 ± 0.184	0.305
36 weeks	0.755 ± 0.246	0.723 ± 0.198	0.649
MAPSE (mm)			
20 weeks	0.427 ± 0.173	0.375 ± 0.089	0.202
28 weeks	0.471 ± 0.190	0.495 ± 0.147	0.331
36 weeks	0.630 ± 0.232	0.617 ± 0.210	1.00
Tricuspid E/A ratio			
20 weeks	0.644 ± 0.070	0.632 ± 0.071	0.477
28 weeks	0.707 ± 0.084	0.703 ± 0.075	0.892
36 weeks	0.718 ± 0.103	0.715 ± 0.099	0.868
Mitral E/A ratio			
20 weeks	0.595 ± 0.082	0.604 ± 0.077	0.503
28 weeks	0.701 ± 0.070	0.681 ± 0.086	0.348
36 weeks	0.708 ± 0.112	0.698 ± 0.095	0.574
Aortic velocity (cm/s)			
20 weeks	63.9 ± 9.53	67.2 ± 10.6	0.102
28 weeks	76.6 ± 11.7	78.4 ± 13.2	0.630
36 weeks	82.2 ± 13.8	88.1 ± 11.5	0.112
Pulmonary artery velocity (cm/s)			
20 weeks	62.5 ± 9.9	63.7 ± 10.5	0.420
28 weeks	74.0 ± 16.6	72.9 ± 13.0	0.833
36 weeks	83.3 ± 15.4	83.0 ± 15.6	0.414

Table 3 *Continued*

Parameter/ gestational age	*Exercise group* (n = *41*)	*Controls* (n = *51*)	P
Ductus arteriosus PI			
20 weeks	2.41 ± 0.391	2.26 ± 0.330	0.077
28 weeks	2.29 ± 0.407	2.40 ± 0.301	0.065
36 weeks	2.51 ± 0.430	2.38 ± 0.295	0.160
Aortic arch PI			
20 weeks	2.58 ± 0.407	2.48 ± 0.326	0.175
28 weeks	2.48 ± 0.369	2.52 ± 0.332	0.316
36 weeks	2.55 ± 0.386	2.52 ± 0.359	0.751
Ejection fraction (%)			
20 weeks	0.814 ± 0.169	0.849 ± 0.119	0.395
28 weeks	0.868 ± 0.093	0.843 ± 0.115	0.464
36 weeks	0.842 ± 0.159	0.785 ± 0.163	0.014

Data are expressed as mean ± SD. E/A, E-wave/A-wave; MAPSE, mitral annular plane systolic excursion; MPI, myocardial performance index; PI, pulsatility index; TAPSE, tricuspid annular plane systolic excursion.

SUPPORTING INFORMATION ON THE INTERNET

The following supporting information may be found in the online version of this article:

Appendix S1 Article of randomized controlled trial by Brik *et al.* published in *Ultrasound in Obstetrics & Gynecology*, with the sections affected by the reclassification of nine patients highlighted in yellow

Fetal and maternal Doppler adaptation to maternal exercise during pregnancy: A randomized controlled trial

Fernández-Buhigas I, Martin-Arias A, Vargas-Terrones M, Brik M, Rollé V, Barakat R, Muñoz Gonzalez MD, Refoyo I, Gil. MM, Santacruz B. J Matern Fetal Neonatal Med. 2023 Dec;36(1):2183759.

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ORIGINAL ARTICLE

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Check for updates

Fetal and maternal Doppler adaptation to maternal exercise during pregnancy: a randomized controlled trial

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ABSTRACT

Background: Regular and supervised exercise during pregnancy is worldwide recommended due to its proven benefits, but, during exercise, maternal blood flow is redirected from the viscera to the muscles and how fetal wellbeing may be affected by this redistribution is still not well known.

Objective: To analyze the longitudinal effect of a supervised moderate physical exercise program during pregnancy on uteroplacental and fetal Doppler parameters.

Methods: This is a planned secondary analysis of an randomized controlled trial (RCT), performed at Hospital Universitario de Torrejón, Madrid, Spain, including 124 women randomized from 12^{+0} to 15^{+6} weeks of gestation to exercise vs. control group. Fetal umbilical artery (UA), middle cerebral artery, and uterine artery pulsatility index (PI), were longitudinally collected by Doppler ultrasound assessment throughout gestation, and derived cerebroplacental ratio (normalized by *z*-score), and maternal mean PI in the uterine arteries (normalized by multiples of the median). Obstetric appointments were scheduled at 12 (baseline, 12^{+0} to 13^{+5}), 20 (19^{+0} to 24^{+2}), 28 (26^{+3} to 31^{+3}) and 35 weeks (32^{+6} to 38^{+6}) of gestation. Generalized estimating equations were adjusted to assess longitudinal changes in the Doppler measurements according to the randomization group.

Results: No significant differences in the fetal or maternal Doppler measurements were found at any of the different checkup time points studied. The only variable that consistently affected the Doppler standardized values was gestational age at the time of assessment. The evolution of the UA PI *z*-score during the pregnancy was different in the two study groups, with a higher *z*-score in the exercise group at 20 weeks and a subsequent decrease until delivery while in the control group it remained stable at around zero.

Conclusions: A regular supervised moderate exercise program during pregnancy does not deteriorate fetal or maternal ultrasound Doppler parameters along the pregnancy, suggesting that the fetal well-being is not compromised by the exercise intervention. Fetal UA PI *z*-score decreases during pregnancy to lower levels in the exercise group compared with the control group.

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Exercise; pregnancy; Doppler; fetal wellbeing; physical activity

Introduction

Regular and supervised exercise during pregnancy is worldwide recommended due to its proven benefits [1]. Certain pregnancy complications such as preeclampsia, gestational diabetes, or increased maternal weight gain could be potentially prevented or improved by the practice of exercise [2–8]. However, during exercise, blood flow is redirected from the viscera to the muscles [9,10] and how fetal wellbeing may be affected by this redistribution is still not well known.

Two findings have been shown when practicing of physical exercise during pregnancy: a transitory fetal bradycardia, followed by a mild compensatory tachycardia, especially at higher exercise intensities [11–14], and an increase in the baseline fetal heart rate [15,16].

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Both fetal cardiac findings return to normal when the exercise is over, suggesting a fetal adaptation to a lower utero-placental perfusion [11]. Additionally, few studies have reported a higher variability in the fetal heart rate trace, that could also reflect a fetal cardiac adaptation to chronic physical activity during pregnancy [17–19].

On the other hand, fetuses exposed to a chronic placental under-perfusion, usually associate some changes in uteroplacental and fetal Doppler parameters that can worsen perinatal outcome and children neurologic development later in life [20–23]. Fetal blood obtained by cordocentesis from small for gestational age fetuses demonstrated that a high pulsatility index (PI) in the umbilical artery (UA) and decreased PI in the fetal middle cerebral artery (MCI) are associated with fetal hypoxemia and acidemia [24–27]. It was also shown that the cerebro-placental ratio (CPR), combined or not with the PI in the uterine arteries, was associated with adverse perinatal outcome not only in small for gestational age but also in normally grown fetuses [28–31]. Therefore, assessing fetal and maternal Doppler measurements in pregnancies where exercise is routinely performed may help to evaluate fetal wellbeing in such cases.

A recent systematic review evaluating the impact of regular maternal physical activity on fetal and neonatal wellbeing in uncomplicated pregnancies, included studies assessing fetal Doppler in pregnancies where exercise was routinely carried out concluded that, although apparently safe, scientific evidence was heterogeneous and insufficient [32].

In a previous randomized controlled trial (RCT), pregnant women were randomly assigned to a supervised exercise program during pregnancy or control, in order to assess maternal weight gain [33]. In this planned secondary analysis, the hypothesis was that fetuses exposed to continuous maternal exercise adapt their cardiovascular system [20,21,34,35]. This adaptation could be translated in a different evolution of fetal and maternal Doppler parameters during pregnancy. Therefore, the main objective was to evaluate the fetal and maternal Doppler adaptation to maternal exercise by comparing longitudinal changes in utero-placental and fetal Doppler measurements performed throughout the pregnancy in both study groups.

Materials and methods

Trial design and participants

This is a planned secondary analysis of an RCT performed at Hospital Universitario de Torrejón, Madrid, Spain, including 124 women randomly assigned into a supervised moderate exercise program during pregnancy or into a control group, who continued with their routine daily activity (NCT 02756143) [33]. It was carried out from November 2014 to June 2015. Briefly, eligibility criteria were uncomplicated pregnancies, less than 16 weeks' gestation who were able to complete the exercise program (to attend >70% of the exercise sessions) if allocated in this group, and who did not meet any exclusion criteria (non-availability to attend to the exercise program during pregnancy or not full filling any of the inclusion criteria) [33,36,37]. For the present analysis, only cases where fetal and maternal Doppler ultrasound assessments were available at any hospital visit were included.

Intervention program

The intervention program was designed following the latest American College of Obstetricians and Gynecologists (ACOG) guidelines and followed the structure of previous studies [5,37–39]. Briefly, the program consisted of a supervised physical conditioning program [40] of three-60-min-sessions per week at the hospital gymnasium from 12^{+3} to 15^{+6} weeks and during the entire duration of the pregnancy or until 39^{+6} weeks of gestation if delivery had not occurred before. Each session included 10 min of warming up, 25 min of cardiovascular exercise, 10 min of strengthening exercises, 5 min of coordination and balance, 5 min of pelvic floor exercises, and 5 min of stretching and relaxation. Aerobic activity was prescribed at moderate intensity, aiming for 55–60% of the age-predicted maximum heart rate reserve (HR), estimated by the Karvonen formula. All women wore an HR monitor (Polar FT7) during the training session to ensure that exercise intensity was moderate and the rating on Borg's Rate of Perceived Exertion Scale at the end of the session should range from 12 to 14 (somewhat hard) [41]. Sessions were conducted twice daily, four days per week and, per protocol, women should join at least three sessions per week.

Weekly volume of physical activity and percentage of assistance to the program were monitored all throughout the pregnancy, by a qualified exercise specialist trained in pre and postnatal exercise.

Control group

Pregnant women allocated to the control group were advised to continue with their routine activity without joining any educational exercise program which included more than 30 min per session at least three times per week. The weekly volume of physical activity was monitored by the exercise specialist at a final interview at 38^{+0} to 39^{+6} weeks of gestation.

Randomization

Randomization was carried out from 12^{+0} to 15^{+6} weeks of gestation. Epidat V.3.1 program was used to perform a simple randomization into two groups (exercise group and control group) using a computer-generated list of random numbers ($n = 200$) in order to create two balanced but not necessarily equal size groups, as previously described [36].

Follow-up

After randomization, both groups followed the same antenatal care at the Hospital. Obstetric appointments were scheduled at 12 (baseline, range 12^{+0} to 13^{+5}), 20 (range 19^{+0} to 24^{+2}), 28 (range 26^{+3} to 31^{+3}), and 35 weeks (range 32^{+6} to 38^{+6}) of gestation. Demographic data were recorded at the 12^{+0} to 13^{+5} weeks' appointment.

The following maternal characteristics were recorded: maternal age, maternal weight at 12^{+0} to 13^{+5} weeks, height, body mass index, ethnicity (Caucasian vs. non-Caucasian), method of conception (natural or assisted conception), cigarette smoking during pregnancy (yes or no), parity (parous or multiparous, according to previous delivery at $\geq$24 weeks' gestation), gestational age in weeks and days from the last menstrual period calculated according to the first trimester ultrasound, and level of physical activity or exercise performed before pregnancy with the Global Physical Activity Questionnaire (GPAQ) (no activity, occasional exercise but not regular, active (twice per week), very active (3–4 times per week), athlete (daily exercise)). Birthweight at delivery was recorded and transformed into centiles [42].

All patients had a final appointment with the exercise specialist at 38^{+0} to 39^{+6} weeks' gestation in other to check their final weight and assess the weekly volume of physical activity (walking minutes per week, domestic labor per week, on foot minutes per week).

Fetal ultrasound assessments were performed using a Voluson S8 (GE Healthcare, Zipf, Austria) ultrasound machine with a convex transducer (RAB6-RS) at every antenatal appointment scheduled. Fetal and maternal Doppler was performed at 20-, 28-, and 35-weeks scans.

Umbilical artery pulsatility index (UAPI), middle cerebral artery pulsatility index (MCAPI), and mean uterine arteries pulsatility index (UtPI), were recorded. The CPR was calculated as MCAPI/UAPI. Fetal Doppler measurements were normalized by *z*-score, and maternal Doppler uterine artery pulsatility index (UtPI) was normalized by multiples of the median (MoMs), calculated at the Fetal Medicine Foundation website [43,44].

Statistical analysis

For this study, a per-protocol analysis was performed, and only women attending to more than 70% of the sessions were included (being 100% assistance when attending all the sessions and 0% when not attending any session).

Descriptive analysis was performed by median (interquartile range, IQR) for continuous variables, and frequency and percentage for categorical variables.

Generalized estimating equations (GEEs) were adjusted to assess the influence of exercise in longitudinal changes of each Doppler measurement for both, the exercise and the control groups while taking into account correlation between different observations of the same patient [45]. Models were also adjusted by walking minutes, on foot time and domestic work per week, removing these variables when they were not significant. To test how the exercise affected the evolution of each Doppler parameter, an interaction between the gestational age and the intervention was evaluated in the models. Coefficients of the regressions and their 95% CI were reported to quantify the association between variables. Normality of residuals hypothesis was verified for all models. A Box-Cox transformation was necessary to ensure normality of the residuals for analysis of UtPI. The number of pregnancies included in each analysis was reported wherever necessary. Level of significance was set at .05.

R software (version 4.0.2) (R Foundation for Statistical Computing, Vienna, Austria) [46] was used for statistical analysis. *Geepack* package was used to adjust the GEE models [47] and *forecast* and *car* packages were used for the Cox-Box transformation [48].

Ethical approval

The study was approved by the Local Research Ethics Committee of the Hospital (CEIC Hospital Universitario Severo Ochoa) (06/07/2013; Madrid, Spain) and was in accordance with the ethical guidelines of the

Declaration of Helsinki (modified in 2008). All women gave written informed consent.

Results

The trial finished prematurely when 124 women had been recruited and randomized into two groups; 70 women were randomized to the exercise group and 54 to the control group. After exclusions, 41 women were included in the exercise group and 51 in the control group for this study (Figure 1). Baseline characteristics were similar in both groups (Table 1). Although there was a similar number of women who smoked before pregnancy in both groups, the proportion of smokers during pregnancy was lower in the exercise group. However, the reduction rate was not significantly different (90.0% in the exercise group compared to 63.6% in the control group, p value = .21).

No significant differences in the fetal or maternal Doppler measurements were found at any of the different checkup time points (Table 2 and eFigures S1–S4).

In the GEE models performed to evaluate repeated measurements, the only variable that consistently affected the Doppler standardized values was gestational age at the time of assessment (eTables S1–S4). The evolution of the UAPI z-score during the pregnancy was different in the two study groups (p value of the interaction = .01), with a higher z-score in the exercise group at 20 weeks and a subsequent decrease until delivery while in the control group it remained stable at around zero (Figure 2, e Table S1).

Discussion

Principal findings

Maternal regular supervised moderate exercise during pregnancy does not deteriorate fetal or maternal Doppler parameters suggesting that fetal wellbeing is not compromised. Fetal UAPI z-score decreases during pregnancy, probably reflecting an improved placental perfusion and fetal oxygenation.

Strengths of the study

The main strength of our study resides in being an RCT with several checkups at different timepoints and with prospectively collected data. Additionally, we followed the international recommendations for exercise during pregnancy when designing the training program, which allows comparisons with other studies and future combination of data.

Limitations of the data

The main limitation of this study relates to the small sample size which might be the reason for the lack of differences found between groups when evaluating the ultrasound assessment performed at each gestational age independently. Although almost 50% of the women were excluded in the intervention group, this

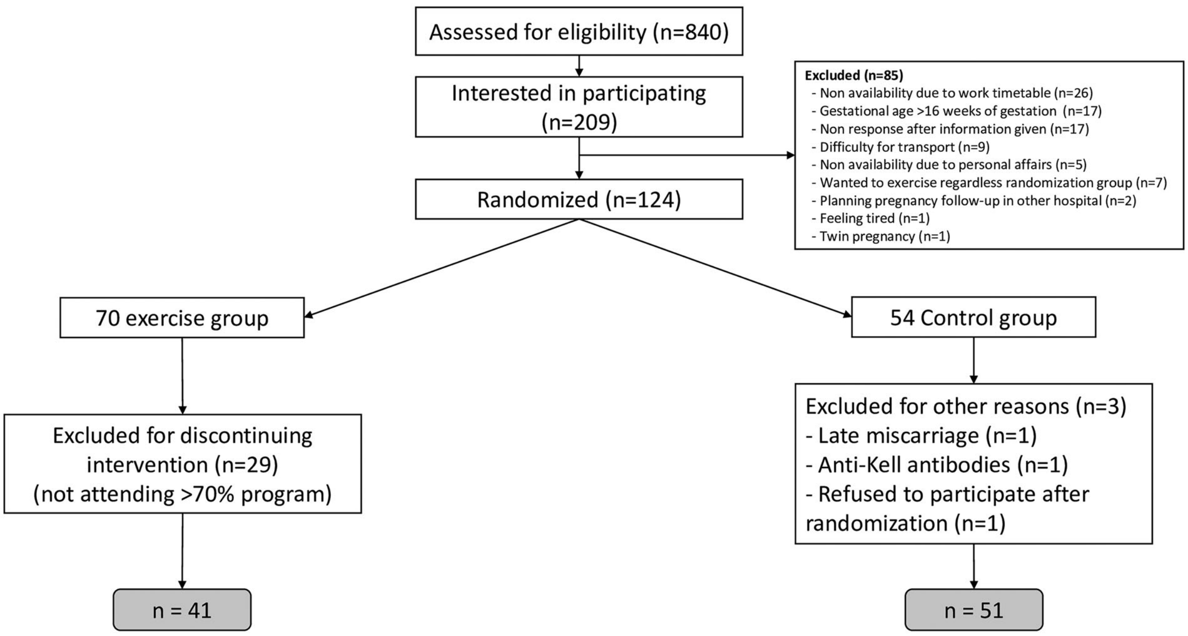

Figure 1. Patients' flow diagram.

Table 1. Maternal and pregnancy characteristics of the study population.

	Control group ($N = 51$)	Exercise group ($N = 41$)
Age (years)	33.0 (30.0, 35.5)	33.0 (31.0, 35.0)
Body mass index (kg/m^2)	23.0 (20.2, 25.4)	21.9 (20.7, 24.0)
Ethnicity		
Caucasian	48 (94.1%)	40 (97.6%)
Latin-American	3 (5.9%)	1 (2.4%)
Conception method		
Natural	48 (94.1%)	40 (97.6%)
Assisted	3 (5.9%)	1 (2.4%)
Previous smoking		
No	29 (56.9%)	31 (75.6%)
Yes	22 (43.1%)	10 (24.4%)
Smoking during pregnancy		
No	43 (84.3%)	40 (97.6%)*
Yes	8 (15.7%)	1 (2.4%)*
Parity		
Nulliparous	38 (74.5%)	31 (75.6%)
Multiparous	13 (25.5%)	10 (24.4%)
Exercise before pregnancy		
No activity	10 (19.6%)	4 (9.8%)
Occasional exercise	18 (35.3%)	11 (26.8%)
Active	16 (31.4%)	13 (31.7%)
Athlete	7 (13.7%)	13 (31.7%)
Other physical activity during pregnancy		
Walking (minutes/week)	240 (130, 420)	240 (120, 450)
Domestic work (minutes/week)	420 (225, 840)	420 (240, 840)
On foot (minutes/day)	180 (120, 300)	180 (150, 278)
Preeclampsia		
No	48 (94.1%)	41 (100%)
Yes	3 (5.88%)	0 (0%)
Hypertension		
No	50 (98.0%)	41 (100%)
Yes	1 (1.96%)	0 (0%)
Fetal birth weight (centile)	28.2 (11.2, 55.3)	32.4 (6.45, 47.7)
Intrauterine growth restriction (<3rd centile)	6 (11.8%)	5 (12.2%)
Small for gestational age (3rd to 10th centile)	7 (13.7%)	8 (19.5%)
Large for gestational age (>95th centile)	2 (3.92%)	0 (0%)
Gestational diabetes		
No	50 (98.0%)	39 (95.1%)
Yes	1 (1.96%)	2 (4.88%)

Results are presented as median (interquartile range) or as frequency (percentage) as appropriate.
*$p < .05$.

is a per protocol analysis and therefore it is unlikely that the results are biased for this reason. Moreover, this small sample size has prevented us to perform any subgroup analyses which could have been of interest. We also acknowledge that there is an increased proportion of nulliparous women as compared to a routine population, which may represent a selection bias. The most likely explanation for the lower uptake in parous women is that they find more difficult to schedule time for exercising. However, we have not found evidence that exercise affects the pregnancy differently according to parity [43]. Another limitation relates to the fact that physical activity in the control group was evaluated at the end of the study, so we cannot ensure that these women did not join any exercise program during pregnancy. However, Doppler patterns encountered in this group are similar to those reported in routine populations [43,49,50]. Although the exclusion of patients without Doppler measurements may represent a selection bias, we do not believe those cases corresponded to patients of any specific characteristics, but they were just random women for whom the researcher forgot to measure any of the Doppler parameters. Finally, only low-risk pregnancy women were included, and therefore the results might not be valid for a higher risk population.

Interpretation

Several studies have evaluated adverse pregnancy outcome on the basis of cord pH or Apgar scores at birth [51,52]. However, such outcome measures are highly influenced by the events occurring during labor and therefore, unlikely to accurately reflect subtle interventions performed during pregnancy. The only outcome of interest would be the long-term follow up of these babies. Until these long-term studies are available, evaluation of fetal Doppler seems to be the best approach to assess fetal wellbeing.

In this study, we have shown that first, basal Doppler parameters were not significantly different between groups at any gestational age, suggesting that fetal

Table 2. Doppler parameters in the two study groups at the 20-, 28-, and 35-weeks' gestation assessments.

	Control group ($N = 51$)	Exercise group ($N = 41$)
Umbilical artery pulsatility index (*z*-score)		
20 weeks' assessment	−0.149 (−0.612, 0.635)	0.545 (−0.149, 1.14)
Missing data	8 (15.7%)	2 (4.9%)
28 weeks' assessment	−0.00300 (−0.628, 0.565)	0.195 (−0.310, 0.463)
Missing data	4 (7.8%)	2 (4.9%)
35 weeks' assessment	0.114 (−0.337, 1.12)	−0.0755 (−0.558, 0.603)
Missing data	5 (9.8%)	1 (2.4%)
Middle cerebral artery pulsatility index (*z*-score)		
20 weeks' assessment	0.103 (−0.684, 0.721)	0.301 (−0.196, 0.773)
Missing data	7 (13.7%)	2 (4.9%)
28 weeks' assessment	2.02 (1.77, 2.36)	2.04 (1.85, 2.23)
Missing data	4 (7.8%)	4 (9.8%)
35 weeks' assessment	1.84 (1.59, 2.10)	1.83 (1.62, 2.12)
Missing data	6 (11.8%)	2 (4.9%)
Cerebral placental ratio (*z*-score)		
20 weeks' assessment	0.146 (−0.511, 0.773)	−0.153 (−0.490, 0.377)
Missing data	8 (15.7%)	3 (7.3%)
28 weeks' assessment	0.438 (−0.519, 1.18)	0.386 (−0.378, 0.888)
Missing data	5 (9.8%)	4 (9.8%)
35 weeks' assessment	−0.293 (−0.880, 0.442)	0.123 (−0.961, 0.536)
Missing data	6 (11.8%)	3 (7.3%)
Mean uterine arteries pulsatility index (MoMs)		
20 weeks' assessment	0.771 (0.693, 0.982)	0.837 (0.672, 1.09)
Missing data	9 (17.6%)	1 (2.4%)
28 weeks' assessment	0.997 (0.915, 1.24)	1.02 (0.835, 1.29)
Missing data	5 (9.8%)	3 (7.3%)
35 weeks' assessment	0.974 (0.858, 1.16)	0.976 (0.829, 1.25)
Missing data	7 (13.7%)	2 (4.9%)

MoMs: multiples of the median.
Results are presented as median (interquartile range).

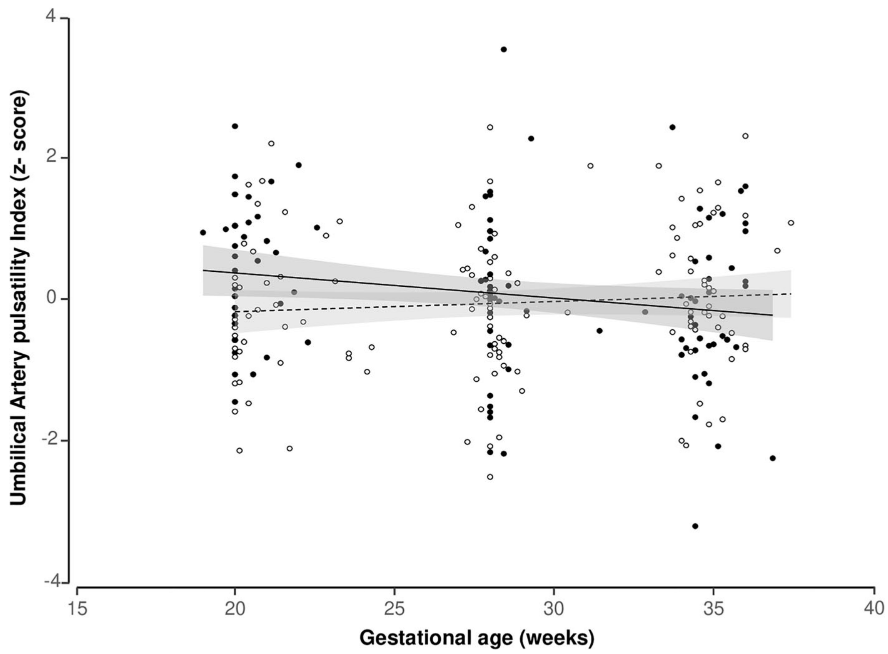

Figure 2. Evolution of the fetal umbilical artery pulsatility index (*z*-score) throughout pregnancy in the control group (empty circles and discontinued grey regression line) and in the exercise group (black circles and black regression line).

wellbeing is not compromised by the exercise; and second, the evolution of the UAPI *z*-score was different between groups, toward an increased placental blood flow from the second to the third trimester in the exercise group as compared to the control group. Since the fetal Doppler indexes are presumably reflecting placental perfusion and oxygenation, it is possible that, during the early stages of exercise, blood is diverted away from the placenta toward other vascular trees, supplying the muscles involved in the exercise. With continuing exercise, as it happens with non-pregnant individuals, an improvement in the maternal cardiovascular system is expected and therefore, there may well be better placental perfusion and fetal oxygenation, reflected as a decrease in the UAPI.

Several small RCTs have studied the effect of chronic exercise [53–56]. However, most of these studies evaluated fetal heart rate, neonatal Apgar scores and birth cord gases to assess fetal wellbeing. There are only three RCTs evaluating the effect of chronic exercise during pregnancy in uteroplacental and fetal Doppler parameters [56–58]. The largest one, compared 54 women who started exercising at 13 weeks' and 60 women who started at 20 weeks' with 57 women who remained sedentary [56] and they did not find any differences. The second study [57] compared 26 women who followed a pelvic floor muscle training from 20 to 36 weeks with 33 women without any intervention, and no differences were found. However, in these two studies, the degree of physical activity was substantially lower than in our study, and results may not be comparable. The third RCT, involved 26 women who underwent a similar exercise program as in the present study, and 26 women who remained sedentary [58]. In this study, women were exposed to a cycle-ergometer test at 34 weeks and fetal and maternal Doppler were assessed before and after the test. No significant differences between groups were found in the UAPI, MCAPI, CPR nor UtPI before the intervention, but UAPI was significantly lower in the exercise group after the cycle-ergometer test. These findings might reflect a better feto-placental adaptation to stressful situations (like acute exercise) in the exercise group, while basal conditions remain unchanged. In contrast, Szymanski and Satin [13] found no differences before and after a peak treadmill test to volitional fatigue according to a modified Balke protocol, in women who did not routinely perform any exercise nor in women normally active, but they did find an increase in the UAPI at high-intensity physical activity. Therefore, they concluded that only high-intensity physical activity may compromise fetal wellbeing. Other studies evaluating acute fetal response to exercise have shown that Doppler modifications due to placental under perfusion are more likely to occur at higher exercise intensities [13,14,59]. In a recent systematic review [32], no adverse effect of chronic maternal physical activity on fetal nor maternal Doppler was found, concluding that maternal exercise during low-risk pregnancy is safe for fetal and neonatal well-being when practiced according to current recommendations. Nevertheless, this meta-analysis included very heterogeneous studies, most of them not randomized and of very small sample size, with different interventions and outcome measures. Therefore, the authors also recommended bigger randomized trials, with similar exercise programs, to better clarify this research question [32].

The general benefits of exercise both in cardiovascular profile and quality of life are well known. Similarly, exercise during pregnancy has shown to prevent the typical pregnancy associated musculoskeletal pain [60,61], to provide a better sleep and to lower the stress and anxiety during pregnancy while decreasing the risk of depression [37,62–64] and adverse perinatal outcome [65–67]. The findings of this study may help encourage expectant mothers to join a specifically designed program, reassuring them about the safeness of exercise during pregnancy. However, more data are needed to further evaluate this hypothesis.

Conclusions

In low-risk pregnancy women, a regular supervised moderate exercise program during pregnancy does not deteriorate fetal or maternal Doppler parameters along pregnancy, reflecting that the exercise practice during pregnancy is safe for the fetus since placental perfusion and fetal oxygenation is conserved. However, further studies are needed to confirm these findings.

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Disclosure statement

No potential conflict of interest was reported by the author(s).

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Maternal physiological changes at rest induced by exercise during pregnancy: A randomized controlled trial

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ABSTRACT

Objective: to analyse maternal physiological changes in several areas (cardiovascular, metabolic, renal and hepatic) related to the regular practice of a supervised exercise program.
Methods: This is an unplanned secondary analysis from a randomized controlled trial carried out in a single maternity unit in Madrid, Spain (NCT 02,756,143). From November 2014 to June 2015, 92 women were randomly assigned to perform a mild-moderate supervised exercise program during pregnancy (Intervention group, IG) or to continue with their routine pregnancy care (control group, CG). For the purpose of this study we collected clinical and analytical data (heart blood pressure, weight, blood glucose, AST, ALT, blood Creatinine and blood Uric acid) available from all obstetric visits and examined the differences between groups.
Results: We did not find any differences in: pregnancy weight (IG: 11.4 ± 4.4 Kg vs. CG: 10.1 ± 5.3 Kg; $p = 0.173$); fasting glucose at 10^{+0}–12^{+6} weeks (IG: 78.48 ± 8.34 vs. CG: 76 ± 13.26, $p = 0.305$) or at 34^{+0}–36^{+4} weeks (IG: 73.25 ± 10.27 vs CG: 73.45 ± 8.29,$p = 0.920$), and 50 gs glucose tolerance at 24^{+4}–26^{+6}weeks (IG: 116.23 ± 35.07 vs CG: 116.36 ± 25.98, $p = 0.984$); Aspartate-amino-transferase at 10^{+0}–12^{+6} weeks (IG: 15.38 ± 4.17 vs CG: 17.33 ± 7.05, $p = 0.124$) and at 34^{+0}–36^{+4} weeks (IG: 21.65 ± 5.25 vs CG: 19.53 ± 8.32, $p = 0.165$) or Alanine-amino- transferase at 10^{+0}–12^{+6} weeks (IG: 27.50 ± 10.63 vs CG: 28.27 ± 11.77, $p = 0.746$) or at 34^{+0}–36^{+4} weeks (IG: 22.93 ± 9.23 vs CG: 20.84 ± 13.49, $p = 0.407$); blood Creatinine concentrations at 34^{+0}–36^{+4} weeks (IG: 0.595 ± 0.401 vs CG: 0.575 ± 0.100, $p = 0.757$) and blood uric acid concentrations at 34^{+0}–36^{+4} weeks (IG: 3.526 ± 0.787 vs CG: 3.262 ± 0.672, $p = 0.218$). Heart blood pressure was similar between groups except at 27^{+0}–28^{+6} weeks, where systolic blood pressure was significantly lower in the CG in comparison to the IG (116.31 ± 10.8 mmHg vs. 120.22 ± 10.3 mmHg, $p = 0.010$).
Conclusion: Regular supervised exercise during pregnancy does not alter normal maternal physiology.

1. Introduction

Regular exercise mediates several physiological modifications in the human being, contributing to the prevention of several illnesses and to the personal wellbeing. In order to prevent obesity and several cardiovascular and metabolic illness, the World Health Organization (WHO) has published a guideline proposing the minimal activity recommended according to ages [1].

Cardiovascular changes at rest have been described in pregnant women that are under a supervised mild-moderate exercise program during pregnancy, like lower heart rate levels or lower heart blood systolic and diastolic pressures [2–5]. This would reflect a positive adaptation of the maternal cardiovascular system to the exercise and it may reduce the risk of preeclampsia during pregnancy [6].

Regarding metabolism, a good supply of nutrients is essential during pregnancy [7]. Exercise increases the use of glucose by the muscles, and it has been shown that a decrease in the blood glucose just occurs for a short period of time during prenatal exercise and, more acutely during

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the third trimester. Additionally, exercise during pregnancy elevates circulating triglyceride levels [8]. It has been reported that acute exercise in pregnant women, as opposed to choric exercise training, is associated with increased sympatho-adrenal and neurohumoral activity [7,9]. On the other hand, regular exercise, during pregnancy reduces glucose levels at the screening test for gestational diabetes (50 gs Glucose Tolerance Test) at 24–28 weeks of gestation [10]. At renal level, no effect has been concluded when performing moderate exercise during pregnancy [8].

Most studies conclude that the regular practice of mild to moderate exercise during pregnancy is not only safe but even positive for both, the mother and the future new-born [4], although the underlying physiological changes are not well established.

The aim of the present study was to analyse physiological changes in the maternal cardiovascular, metabolic, renal and hepatic systems, in relation to the regular practice of a supervised mild-moderate exercise program. We hypothesized that this exercise during pregnancy would not alter the normal maternal physiology.

2. Methods

2.1. Trial design and participants

This is an unplanned secondary analysis of a randomized controlled trial (RCT), performed at the Hospital Universitario de Torrejon, Madrid, Spain (NCT 02,756,143). A complete description of the design and methods of this RCT, was recently published [11]. Our main Objective was to clarify if performing a supervised controlled exercise program throughout pregnancy prevented excessive gestational weight gain. From November 2014 to June 2015, we included a total of 124 pregnant women.

Inclusion criteria were: (I) no obstetric complications according to the American College of Obstetricians and Gynaecologists (ACOG) guidelines [12], (II) gestational age at recruitment < 16 weeks, (III) not exercising regularly for more than 30 min (3 days per week), and (IV) able to communicate in Spanish. Exclusion criteria were non-availability to attend to the exercise program during pregnancy or not full filling any of the inclusion criteria.

A simple randomisation was performed with the *Epidat V.3.1* program to allocate the participants into two groups in order of entry: intervention group (IG) and control group (CG). For this, a computer-generated list of random numbers ($n = 200$) was created through the *Epidat* option of balanced groups (similar but not of equal size). Unfortunately, due to the lack of resources, the target number of participant could not be achieved.

Trial coordinators regularly undertook quality control of data handling, and verification of adherence to protocols.

The study was approved by the Local Research Ethics Committee (CEIm Hospital Universitario Severo Ochoa) (19/07/2013). All women gave written consent.

2.2. Maternal and pregnancy characteristics

We recorded the following maternal characteristics: maternal age, maternal weight at 12^{+0}–13^{+5} weeks and height, Body mass index (BMI), racial origin (Caucasian vs non-Caucasian), method of conception (natural or assisted conception), cigarette smoking during pregnancy (yes or no), parity (parous or, according to previous delivery at ≥ 24 weeks' gestation) and gestational age at delivery in days from the last menstrual period calculated by ultrasound.

2.3. Control group

Pregnant women allocated to the CG were advised to do normal daily activity and not to join any educational exercise program including more than 30 min per day at least 3 times per week. The weekly volume of physical activity was monitored by an exercise specialist at a final interview at 38^{+0}–39^{+6} weeks of gestation.

2.4. Intervention programme

The intervention programme was designed according to the 2015 ACOG standards and followed the structure of previous programme studies [12–15]. It consisted in a supervised physical conditioning programme of three-60-minutes-sessions per week during the whole pregnancy (from 12^{+3}–15^{+6} weeks to 38^{+0}–39^{+6} weeks of gestation) at the Hospital gym. Women could attend any of the two evening sessions we offered four days per week, up to a total of three. Each session included 10 min of warming up, 25 min of cardiovascular exercise, 10 min of strengthening exercises, 5 min of coordination and balance, 5 min of pelvic floor exercises and 5 min of stretching and relaxation. Exercises in the supine position were not performed for more than 2 min. Aerobic activity was prescribed at mild to moderate intensity, aiming for 55–60% of maximum heart rate (HR). All women wore a HR monitor (Polar FT7) during the training session to ensure that exercise intensity was mild-moderate and the rating of perceived exertion scale ranged from 12 to 14 (Somewhat Hard) [16].

Weekly volume of physical activity and the percentage of assistance to the program were monitored all throughout the pregnancy by a qualified exercise specialist trained in pre and postnatal exercise.

2.5. Follow-up

Once recruited, both groups had a similar follow-up at the Hospital Universitario de Torrejon. Obstetric appointment took place at 12^{+0}–13^{+5}, 19^{+0}–21^{+6}, 27^{+0}–28^{+6} and 35^{+0}–36^{+6} weeks of gestation. Maternal blood pressure and maternal weight were checked in every visit. Measurements taken at 12^{+0}–13^{+5} week´s appointment were considered as the baseline measurements. Patients were randomized until 15^{+6} weeks of gestation. All patients had a final interview with the exercise specialist at 38^{+0}–39^{+6} weeks´ gestation in other to check their final weight and assess weekly volume of physical activity.

Routine blood routine tests were performed fasting at 10^{+0}–12^{+6} and 34^{+0}–36^{+4} weeks, and not fasting at 24^{+4}–26^{+6} weeks, always in the morning.

Microlife WatchBP Home blood pressure monitor was used for blood pressure assessment. Blood pressure was measured after 5 min of rest in a sitting position, with the arm resting at the level of the heart. Maternal weight was measured in an automatic SECA scale. Blood samples for glucose, Aspartate-amino-transferase (AST), Alanine-amino-transferase (ALT), creatinine and uric acid, were analysed by Dimension EXL (Siemens).

2.6. Study outcomes

Study outcomes were verified by one of three members of the research team (I.F.B., M.B. or A.M.) and are summarized in the following list according to the organ studied.

2.6.1. Cardiovascular

Maternal systolic and diastolic blood pressure measured in mmHg, after 5 min of rest, in sitting resting position, in one arm at heart level, checked at 12^{+0}–13^{+5} (baseline), 19^{+0}–21^{+6}, 27^{+0}–28^{+6} and 35^{+0}–36^{+6} weeks in the obstetric appointment.

2.6.2. Metabolic and hepatic

Maternal weight measured (Kg), checked at 12^{+0}–13^{+5} (baseline), 19^{+0}–21^{+6}, 27^{+0}–28^{+6}, 35^{+0}–36^{+6} and at 38^{+0}–39^{+6} (final weight). Pregnancy weight gain was calculated as the final maternal weight minus the baseline weight.

Fasting blood glucose levels (mg/dl) were measured at the 10^{+0}–12^{+6}- and 34^{+0}–36^{+4} weeks routing blood tests. Blood glucose levels 60 min after a 50 mg Glucose Tolerance Test were measured at the 24^{+4}–26^{+6} weeks routine blood test.

Alanine-amino-transferase (ALT) and Aspartate-amino-transferase (AST) were measured at the 10^{+0}–12^{+6} and 34^{+0}–36^{+4} weeks routine blood test (UI/l) to asses hepatic function and amnio acid metabolism, respectively.

2.6.3. Renal

Serum creatinine and uric acid levels (mg/dl) were determined at the 34^{+0}–36^{+4} weeks routine blood test to asses renal function. Our protocol did not include any earlier analysis.

2.7. Statistical analysis

To describe demographic and clinical characteristics of patients, data were expressed as mean (standard deviation) or median (interquartile range), and proportions (absolute and relative frequencies) as appropriate. Comparisons between treatment groups were performed by unpaired t-Student test, Mann-Whitney *U test* or two-tailed $\chi 2$-test as appropriate. The statistical software package SPSS (IBM Corp. Released 2012. IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY: IBM Corp) was used for data analysis.

3. Results

A total of 124 women were recruited and randomized into two groups. Seventy pregnant women were randomised to the intervention group (IG) and 54 to de control group (CG). Three women were excluded from the CG: one woman because of a late miscarriage at 20 weeks, other because of high-risk pregnancy (anti-kell antibodies), and the third one withdrew consent after randomization. Additionally, one woman from the IG had non available blood tests results. Twenty-eight women from IG were not compliant with the programme and attended <70% of the programme as requested by the study protocol. A per protocol analysis was finally made with the two final groups: IG (N = 41) and CG (N = 51), as shown in the Trial Profile (Fig. 1).

The baseline characteristics were similar in both groups. Regarding maternal age, pre-pregnancy BMI, parity, IVF pregnancy, ethnic, previous to pregnancy physical exercise and smoking, both groups were homogeneous (Table 1).

Table 1
Demographic characteristics in both groups.
Data are given as mean and Standard deviation (SD) or n (%). Comparisons between outcome groups were by chi, square test for categoric variables and Mann, Whitney U test for continuous variables.

	Intervention Group (N = 41)	Control Group (N = 51)	p value
Maternal age (years)	33.17 (3.19)	32.63 (4.66)	0.510
Maternal 12^{+0}–13^{+5} weeks weight (Kg)	63.65 (10.90)	66.10 (14.56)	0.380
Maternal height (cm)	164.68 (6.89)	164.14 (5.84)	0.682
12^{+0}–13^{+5} weeks BMI	22.81 (3.54)	23.80 (5.09)	0.293
IVF pregnancy	1 (2.4)	2 (3.9)	0.611
Caucasian	41 (100.0)	47 (92.2)	0.067
Pre-pregnancy physical exercise	37 (90.2)	41 (80.4)	0.191
Nulliparous	31 (75.6)	38 (74.5)	0.904
Smoking	10 (24.4)	22 (43.1)	0.061
Gestation time at delivery (days)	278.76 (9.45)	276.08 (11.45)	0.232

Table 2
Cardiovascular outcomes in both groups.
Data are given as mean (Standard deviation). Comparisons between outcome groups were by chi, square test for categoric variables and Mann, Whitney U test for continuous variables.

	Systolic Blood Pressure (mmHg) Intervention Group (N = 41)	Control Group (N = 51)	p value
12^{+0}–13^{+5} Week	120.54 (10.56)	119.51 (11.26)	0.656
19^{+0}–21^{+6} Week	123.08 (8.99)	120.14 (14.10)	0.254
27^{+0}–28^{+6} Week	122.20 (10.31)	116.31 (10.80)	0.010
35^{+0}–36^{+6} Week	121.27 (8.49)	119.18 (14.60)	0.422
	Diastolic Blood Pressure (mmHg) Intervention Group (N = 41)	**Control Group (N = 51)**	**p value**
12^{+0}–13^{+5} Week	72.65 (8.70)	73.05 (7.20)	0.813
19^{+0}–21^{+6} Week	72.96 (10.48)	72.25 (6.88)	0.712
27^{+0}–28^{+6} Week	70.92 (11.03)	73.12 (6.90)	0.269
35^{+0}–36^{+6} Week	75.33 (10.81)	74.46 (6.31)	0.653

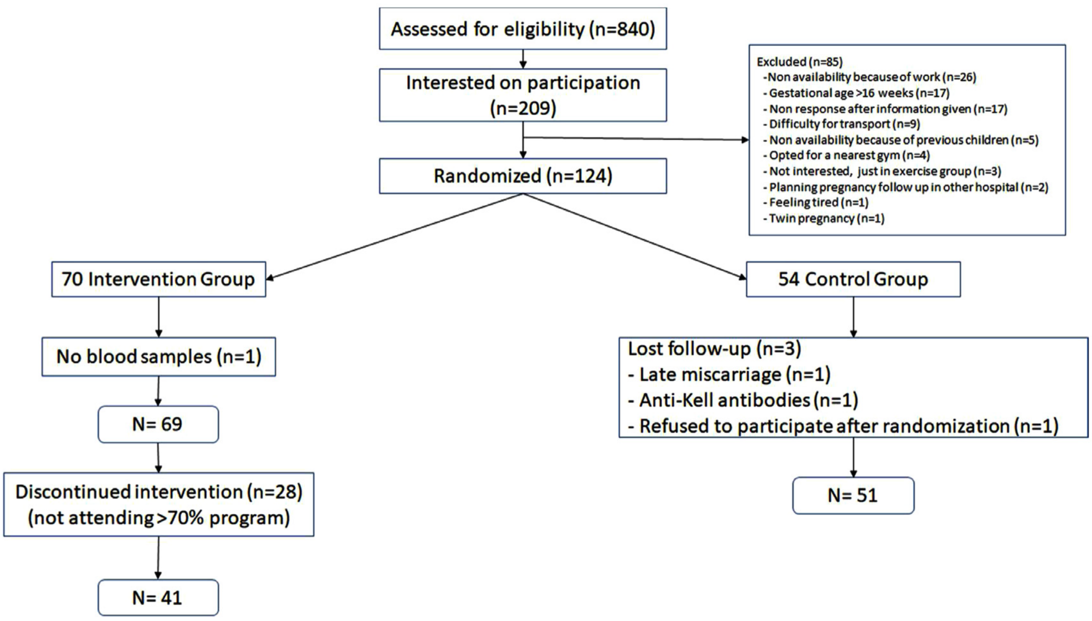

Fig. 1. Flow diagram.

Table 3
Metabolic, Hepatic and renal outcomes in both groups.
Data are given as mean (Standard deviation). Comparisons between outcome groups were by chi, square test for categoric variables and Mann, Whitney U test for continuous variables.

	Weight (Kg) Intervention Group ($N = 41$)	Control Group ($N = 51$)	p value
12^{+0}–13^{+5} Week	64.89 (11.15)	64.34 (18.65)	0.867
19^{+0}–21^{+6} Week	67.96 (10.66)	70.11 (14.50)	0.430
27^{+0}–28^{+6} Week	71.46 (11.13)	73.66 (14.70)	0.429
35^{+0}–36^{+6} Week	74.48 (11.54)	76.85 (15.05)	0.411
38^{+0}–39^{+6} Week	75.15 (11.57)	76.25 (15.47)	0.705
Maternal weight gain	10.153 (5.39)	11.49 (4.43)	0.173
	Glucose (mg/dl) Intervention Group ($N = 41$)	**Control Group ($N = 51$)**	**p value**
10^{+0}–12^{+6} Week	78.48 (8.34)	76.00 (13.26)	0.305
24^{+4}–26^{+6} Week, 50 g Glucose Tolerance Test	116.23 (35.07)	116.36 (25.98)	0.984
34^{+0}–36^{+4} Week	73.25 (10.27)	73.45 (8.29)	0.920
	AST (UI/ml) Intervention Group ($N = 41$)	**Control Group ($N = 51$)**	**p value**
10^{+0}–12^{+6} Week	15.38 (4.17)	17.33 (7.05)	0.124
34^{+0}–36^{+4} Week	21.65 (5.25)	19.53 (8.32)	0.165
	ALT (UI/ml) Intervention Group ($N = 41$)	**Control Group ($N = 51$)**	**p value**
10^{+0}–12^{+6} Week	27.50 (10.63)	28.27 (11.77)	0.746
34^{+0}–36^{+4} Week	22.93 (9.23)	20.84 (13.49)	0.407
	Creat (mg/dl) Intervention Group ($N = 41$)	**Control Group ($N = 51$)**	**p value**
34^{+0}–36^{+4} Week	0.595 (0.401)	0.575 (0.100)	0.757
	Uric Acid (mg/dl) Intervention Group ($N = 41$)	**Control Group ($N = 51$)**	**p value**
34^{+0}–36^{+4} Week	3.526 (0.787)	3.262 (0.672)	0.218

3.1. Cardiovascular outcomes

Both systolic and diastolic blood pressure were studied (Table 2) and no differences were found except at 28 weeks, were systolic blood pressure was lower in the CG compared to the IG (116.31 ± 10.8 mmHg vs. 120.22 ± 10.3 mmHg, $p = 0.010$), but always within normal ranges.

3.2. Metabolic and hepatic outcomes

The evolution through gestation of the maternal weight was analysed and no differences were found between groups (Table 3).

When analysing maternal weight gain during pregnancy, no difference was found. However, there was a tendency for a lower maternal weight at the end of the pregnancy in the IG compared to the CG (10.1 ± 5 Kg vs. 11.4 ± 4 Kg, $p = 0.173$) (Table 3).

Fasting blood glucose level in the first and third trimester, blood glucose after 50 mg glucose tolerance test, AST and ALT levels were similar in both groups (Table 3).

3.3. Renal outcomes

Creatinine and uric acid concentrations in the third trimester were similar in both groups (creatinine 0.57 ± 0.1 mg/dl in the IG compared to 0.59 ± 0.4 mg/dl in the CG, $p = 0.757$; uric acid 3.26 ± 0.6 mg/dl in the IG compared to 3.45 ± 0.7 mg/dl in the CG, $p = 0.218$) (Table 3).

4. Discussion

4.1. Main findings of the study

In this study we found that, first renal, metabolic and hepatic metabolism was similar in pregnant women performing a moderated supervised exercise program compared to controls.

Second, although maternal blood pressure was similar between groups, systolic blood pressure was higher at 27^{+0}–28^{+6} weeks´in pregnant women performing a mild-moderated supervised exercise program compared to controls.

And third, pregnancy weight gain tended to be lower in the exercise group, although we were unable to prove significance.

4.2. Cardiovascular outcomes

Cardiovascular changes have been described in pregnant women under a supervised exercise program during pregnancy [17,18]. Perales et al. [19] described that, pregnant women under a supervised mild exercise program, have significant lower heart rate levels, lower blood systolic and diastolic pressure. Moreaver, a randomized controlled study [5] found that aerobic exercise reduced resting systolic blood pressure in normotensive pregnant women and reflected a positive adaptation of the maternal cardiovascular system. Little is known about the mechanism by which exercise may reduce blood pressure during pregnancy. Exercise has been proposed to reduce oxidative stress, improve endothelial function, as well as immune and inflammatory responses [20,21]. In addition, exercise is associated with an increase on the cardiac output [21]. In our study we were unable to show this effect; in contrast, we found the systolic blood pressure to be higher in the IG at 27^{+0}–28^{+6} weeks. Since this finding sounds clinically implausible, we believe that it merely reflects the result of performing multiple comparisons, more than a real effect of the treatment, unless proven otherwise in another study.

4.3. Metabolic and hepatic outcomes

Maternal weight gain during pregnancy has an impact on the pregnancy and on the future newborn [22–33]. Previous meta-analysis have demonstrated that exercise can help to prevent excessive weight gain during pregnancy [34–36]. In our study, no differences were found in maternal weight during each visit during pregnancy or in the maternal weight gain at the end of the pregnancy, although a tendency to a lower pregnancy weight gain could be observed in the intervention group. It is true that if we could stratify by basal BMI we may see more pronounced differences in the higher basal BMI group, as demonstrated by some studies [12,37–44], but this sub-group analysis was not possible due to the small sample size.

Glucose is essential for foetal wellbeing [7]. Exercise increases the capitation of glucose by the muscles, and therefore we could argue that the hypoglycaemia that occurs during exercising mothers may influence foetal growth or development. However, our results show no differences in the basal fasting glucose levels between groups. On the other hand, Barakat et al. [10] and Deierlein et al. [45] concluded that regular exercise during pregnancy reduces glucose levels at the screening test for gestational diabetes at 24–28 weeks of gestation (50 g Glucose Tolerance Test), but our results were are not consistent with this finding. This may be due to the fact that our pregnant women were advised to have a light breakfast before attending the test, while in these studies the test was performed fasting. Some studies suggest that exercise during pregnancy does not prevent from gestational diabetes but can help to control glucose levels in diabetic pregnant women [46–48]. In our study, only one woman developed gestational diabetes in the CG, and therefore no comparison could be carried out at this level.

Regarding the hepatic metabolism, it has been described that exercise increases the levels of AST and its activity [49,50]. During pregnancy, it has not been determined how exercise could affect AST and ALT yet. Our results show no statistical changes in the hepatic enzymes during pregnancy in those women exercising compared to controls.

4.4. Renal outcomes

At a renal level, there is no significant effect when performing mild-moderate exercise during pregnancy [8], although it is not clear whether urinary urea nitrogen excretion could be affected by the exercise [51]. Our results at this point are consistent with this finding, but nitrogen excretion was not measured in our study population.

4.5. Study strengths and limitations

The main strength of our study resides in being a randomized controlled study with multiple timepoints check-ups. Additionally, the guidelines for exercise followed here are internationally recommended.

On the other hand, the main limitation is the small sample size which may be reason for the lack of beneficial results and did not allow us to perform sub-group analyses. Some may argue that increasing exercise intensity may cause a greater impact, however, high-intensity exercise during pregnancy is related to adverse obstetric outcomes and therefore not recommended [52–56]. Another limitation is the increased proportion of nulliparous women compared to the general low risk pregnant population, which could represent a selection bias. However, parity has not been demonstrated as a risk factor for any of the variables studied. Finally, our study included only low-risk pregnancies and therefore our results might not be valid for a different population.

5. Conclusions

A regular supervised mild-moderate exercise programme during pregnancy does not impact the normal physiological changes that occur during pregnancy. However, further and larger studies are needed to confirm our findings.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.physbeh.2020.112863.

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Does Exercise During Pregnancy Affect Placental Weight?: A Randomized Clinical Trial

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Abstract

Placental weight (PW) is a measure commonly used to summarize growth and aspects of placental function. In a normal pregnancy, it is reasonable to assume that PW is related to aspects of the functional capacity of the placenta. The placenta, as the site for all maternal–fetal oxygen and nutrient exchange, influences birth weight and is thus central to a successful pregnancy outcome. PW is the most common way to characterize placental growth, which relates to placental function. With physical exercise becoming an integral part of life for many women, the question of whether exercise during pregnancy has an adverse effect on the growing fetus is very

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important. The aim was to examine the influence of an aerobic exercise program throughout pregnancy on PW among healthy pregnant women. A randomized control trial was used (registration trial number: NCT02420288). Women were randomized into an exercise group (EG; $n = 33$) or a control group (CG; $n = 32$) that received standard care. The EG trained 3 days/week (55–60 min/session) from gestational Weeks 9–11 until Weeks 38–39. The 85 training sessions involved aerobic, muscular and pelvic floor strength, and flexibility exercises. PW and other pregnancy outcomes were measured. There was high attendance to the exercise program, and no differences in the PW at delivery were observed between study groups (CG = 493.2 $\pm$ 119.6 g vs. EG = 495.4 $\pm$ 150 g, $p = .95$). A regular, supervised exercise program throughout pregnancy does not affect the PW in healthy pregnant women.

Keywords
exercise, pregnancy, outcomes, placental weight, newborn

In the past three decades, an increasing amount of evidence has been published on the clinical significance of placental weight (PW) and its long-term effects on health and disease in adult life (Almog et al., 2011; Naeye, 1987; Pardi, Marconi, & Cetin, 1997; Thornburg, O'Tierney, & Louey, 2010). Furthermore, the placenta metabolizes and absorbs nutrients; thus, it is more than a passive conduit. Nutrient transport should be considered a staple of the normal exchange between the maternal body and fetal environment (Hay, 1994).

PW is a measure commonly used to summarize growth and aspects of placental function. In a normal pregnancy, it is reasonable to assume that PW is related to aspects of the functional capacity of the placenta (Salafia, Charles, & Maas, 2006). In fact, to a large degree, the placenta translates how the fetus experiences the maternal environment and, genetic influences aside, is the principal influence on one of the most important pregnancy outcomes: the weight of the newborn (Godfrey, 2002; Salafia et al., 2008; Thame, Osmond, Bennett, Wilks, & Forrester, 2004; Thame, Osmond, Wilks, Bennett, & Forrester, 2001).

Many studies indicated that PW was related to pregnancy outcome (Eskild, Romundstad, & Vatten, 2009; Roland et al., 2012; Shehata et al., 2011). High placenta weight was associated with a poor perinatal outcome, a low Apgar score, respiratory distress, and perinatal death, whereas a low PW was associated with medical complications of the mother. To determine high and low PW, above and below the 10th and the 90th percentiles, respectively, are used (Janthanaphan, Kor-Anantakul, & Geater, 2006). Placentas over 750 g and less than 350 g are unlikely to be normal (Kaplan, 2008). Also, both small and large placentas relative to birth weight (BW) were associated with fetal death in preterm births (Haavaldsen, Samuelsen, & Eskild, 2013).

The idea that PW is an expression of the intrauterine environment is supported by numerous studies (Godfrey, 2002; Haavaldsen et al., 2013; Hendricks, 1964; Salafia et al., 2008). Environmental challenges that disrupt maternal life will impact the fetal environment and transmit across the placenta. The placenta responds to alterations in the maternal–fetal exchange with a wide range of structural and functional changes such as race, socioeconomic problems, or health problems (Perry, Beevers, Whincup, & Bareford, 1995), including changes in PW (Baptiste-Roberts et al., 2008; Fowden, Forhead, Coan, & Burton, 2008; Jansson & Powell, 2007; McNamara, Hutcheon, Platt, Benjamin, & Kramer, 2014).

Thus, maternal factors known to influence fetal growth, BW, and neonatal body composition are also important determinants of PW (Roland et al., 2012). Because certain studies have shown that physical exercise could influence BW (Baciuk, Pereira, Cecatti, Braga, & Cavalcante, 2008; Barakat et al. 2016; Hopkins, Baldi, Cutfield, McCowan, & Hofman, 2010; Ruiz et al, 2013), it is interesting from the scientific point of view to examine the effects of supervised and regular exercise throughout pregnancy on PW.

In this sense, although many studies about the impact of exercise during pregnancy on PW exist (Bergmann, Zygmunt, & Clapp, 2004; Clapp, 2003; Clapp, Kim, Burciu, & Lopez, 2000; Hilde, Eskild, Owe, Bø, & Bjelland, 2017), this relationship has not yet been studied by any Randomized Clinical Trial (RCT).

The aim of the present study was to examine the influence of an exercise program throughout pregnancy on PW among healthy pregnant women.

Based on a previous study (Juhl, Olsen, Andersen, Nøhr, & Andersen, 2010), we hypothesized that maternal exercise would decrease PW.

Material and Method

The present RCT (registration trial number: NCT02420288) was conducted between January 2014 and January 2016 following the ethical guidelines of the Declaration of Helsinki that was last modified in 2000. The research protocol was reviewed and approved by the Hospital Universitario de Torrejón (Madrid, Spain).

We contacted a total of 92 Spanish pregnant women (who descended from three or more generations of Caucasians) from the consultant obstetrician hospital. Only women without any obstetric complications according to the American College of Obstetricians and Gynecologists guidelines (ACOG, 2015) with a singleton gestation and who were not participating in any other trials or exercise programs at the moment of inclusion and throughout pregnancy were invited to participate in this study.

For practical reasons, women who were not planning to give birth at the same obstetric hospital department (Hospital Universitario de Torrejón, Madrid, Spain) and who did not receive medical follow-ups throughout the entire pregnancy period were not included in the study. We also excluded women who had any serious medical conditions that would have prevented them from exercising safely (i.e., long-term muscle injuries). All of the participants provided signed written informed consent prior to participating in the study.

A simple randomization process was used to allocate the study participants. A computer-generated list of random numbers was used to allocate the participants into two groups: exercise and control. The randomization and blinding (sequence generation, allocation concealment, and implementation) were performed by three different authors.

Exercise Intervention

The exercise program was designed following the ACOG (2015) guidelines to ensure that it was safe and effective for pregnant women and included a total of three 55–60 min sessions, performed 3 times per week on alternate days, which lasted from the beginning of the pregnancy (Weeks 8–11) until the end of the third trimester (Weeks 38–39). An average of 85 training sessions was planned. Each exercise session was preceded and followed by a gradual warm-up and cooldown period (both 10- and 12-min duration) and consisted of walking and light static stretching of most muscle groups. The cooldown period included relaxation exercises.

The women wore heart rate monitors (Accurex Plus, Polar Electro OY, Finland) during all sessions to meet the intensity target of 55–60% of their heart rate reserve using the Karvonen equation (Goldberg, Elliot, & Kuehl, 1988). Borg's Rate of Perceived Exertion Scale was also used and ranged from 10 to 12 (*fairly light* to *somewhat hard*, respectively; O'Neill, Cooper, Mills, Boyce, & Hunyor, 1992). During the first week of the program, the pregnant women received a complete explanation and practice of the Borg's scale in order to gain familiarity with this instrument.

After the warm-up, the women participated in different activities, the main objective of which was to reach and hold 55–60% heart rate reserve of intensity for 20–25 min. To achieve this goal, aerobic exercises consisted of low-impact aerobic dance, involving the upper and lower limbs using different musical style choreography. Some specific exercises were then performed to increase muscle strength and to improve balance and to prevent some muscle imbalances that are common among pregnant women (pectoral, back, shoulder, and upper and lower limb muscles). Exercises were performed through the full range of motion. One set (10–12 repetitions) was conducted using barbells (2 kg/exercise) or low-to-medium resistance (elastic) bands (Therabands) and included biceps curls, arm extensions, arm side lifts, shoulder elevations, bench presses, seated lateral row, lateral leg elevations, leg circles, knee extensions, knee (hamstring) curls, and ankle flexions and extensions. The session also included 10 min of pelvic floor muscle training to prevent urinary incontinence.

Extreme stretching, joint overextension, the Valsalva maneuver, ballistic movements, and jumps were avoided, and exercises performed in the supine position on the mat were not performed for more than 2 min.

To maximize program safety, adherence, and efficacy, all sessions were (i) supervised by a qualified fitness specialist (working with groups of 10–12 subjects) and with an obstetrician's assistance, (ii) accompanied by music, and (iii) performed in the Health Care Center in a spacious, well-lit room under favorable environmental conditions (altitude = 600 m, temperature = 19–21°C, and humidity = 50–60%). An adequate intake of calories and nutrients was confirmed before the start of each exercise session.

Usual Care (Control) Group

Women randomly assigned to the usual care (control) group received general advice from their midwife about the positive effects of physical activity. Participants in the usual care group had their usual visits with health-care providers (midwives, obstetricians, and family doctors) during pregnancy at a frequency equal to the exercise group (EG). The women were not discouraged from exercising on their own. They reported no regular exercise during their pregnancies (telephone interviews).

Outcome Measurements

Demographic information was obtained at admission to the study. Medical history and pregnancy outcomes were obtained from medical records. The women's weight and height were measured at admission following standard procedures. Body mass index (BMI) was calculated as weight (kg)/height (m^2), and the women were classified as underweight (BMI < 18.5 kg/m^2), normal weight (BMI ≥ 18.5–24.9 kg/m^2), overweight (BMI ≥ 25–29.9 kg/m^2), and obese (BMI ≥ 30 kg/m^2; Institute of Medicine [IOM], 2009).

Primary outcome. The placentas were always weighed with the membranes and 1 cm of umbilical cord attached by the same specialists (three midwives). All the placentas were weighed during the first 30 min after delivery, an electronic scale was used (NAHITA 5041/5000, weight range 0–5,000 gr).

Secondary outcomes. Other maternal and fetal outcomes, such as gestational age, type of delivery (natural, instrumental, or caesarean), BW, Apgar score (at 1 and 5 min), gestational diabetes, and hypertension, were obtained from perinatal obstetric records. Gestational weight gain was classified according to the 2009 IOM guidelines. The recommended weight gain for underweight, normal weight, overweight, and obese women are 12.5–18 kg, 11.5–16 kg, 7–11.5 kg, and 5–9 kg, respectively (IOM, 2009).

Statistical Analysis

The comparison between treatment groups was performed with Student's t test for unpaired data and the χ^2 test for continuous and nominal data, respectively. We performed all of our analyses using the intention-to-treat principle (Detry & Lewis, 2014), if the outcome value was missing for a participant (lost to follow-up), then we inserted the mean value for that outcome.

Regarding the calculation of sample size, we used a conservative approach. We performed a power calculation for the primary outcome, PW, assuming a bilateral alternative and considering a standard deviation of 89 g based on a previous study (Janthanaphan et al., 2006). Additionally, we wanted to detect differences in PW of at least 70 g with a power of $>80\%$ and α of .05. Assuming a maximum loss at follow-up of 15%, we decided to recruit at least 30 participants for each study group.

The statistical analyses were performed with the Statistical Package for Social Sciences software (Version 20.0 for Windows; SPSS Inc., Chicago, IL). The level of significance was set to $\alpha = .05$.

Results

There were no major adverse effects and no major health problems observed in the participants. In the control group (CG), a total of eight women were lost to follow-up due to the threat of a premature delivery ($n = 2$), a move to another hospital ($n = 3$), or personal reasons ($n = 3$). In the EG, a total of three women were lost to follow-up due to the threat of a premature delivery ($n = 1$), discontinued intervention ($n = 1$), or personal reasons ($n = 1$). However, due to the intention-to-treat, the final number of participants included in the analysis was 32 in the CG and 33 in the EG (Figure 1). No participants changed from one group to the other, and there were no protocol deviations from the study plans. Adherence to the training program was >85% in the experimental group that was measured by a qualified fitness specialist using a checklist of attendance for each session.

The baseline maternal characteristics of both study groups are shown in Table 1. We found no significant differences ($p > .05$) between the groups in maternal characteristics that could potentially influence the main study outcome, PW.

Table 2 shows no differences in the PW at delivery (CG = 493.2 $\pm$ 119.6 g vs. EG = 495.4 $\pm$ 150 g, $p = .95$) and other pregnancy outcomes between the study groups. In the CG, 5 (15.7%) women presented low, 26 (81.2%) women presented normal, and 1 (3.1%) presented with high PWs, respectively. In the EG, the number with low PW was 4 (12.1%), 26 (78.8%) had normal weight, and 3 (9.1%) had high PWs ($p = .57$). Also, regarding the PW:BW ratios, we found no differences between the groups (CG = 0.158 $\pm$ 0.03 vs. EG = 0.157 $\pm$ 0.03, $p = .96$). When we examined the maternal weight gain (MWG) during pregnancy, we also observed no statistical differences between the groups regarding total weight gain (CG = 11.8 $\pm$ 4.8 kg vs. EG = 10.9 $\pm$ 2.7 kg) and the number of women who exceeded their recommended weight gain during pregnancy according to their previous BMI (CG = 8/25% vs. EG = 4/12.1%; $p = .43$ and $p = .18$, respectively).

Additional analysis examining the placenta weight categories (low/normal/high) in relation to MWG during pregnancy (adequate/excessive) also showed no significant differences.

Discussion

The aim of the present study was to examine the effects of an exercise program during pregnancy on PW among healthy pregnant women. The

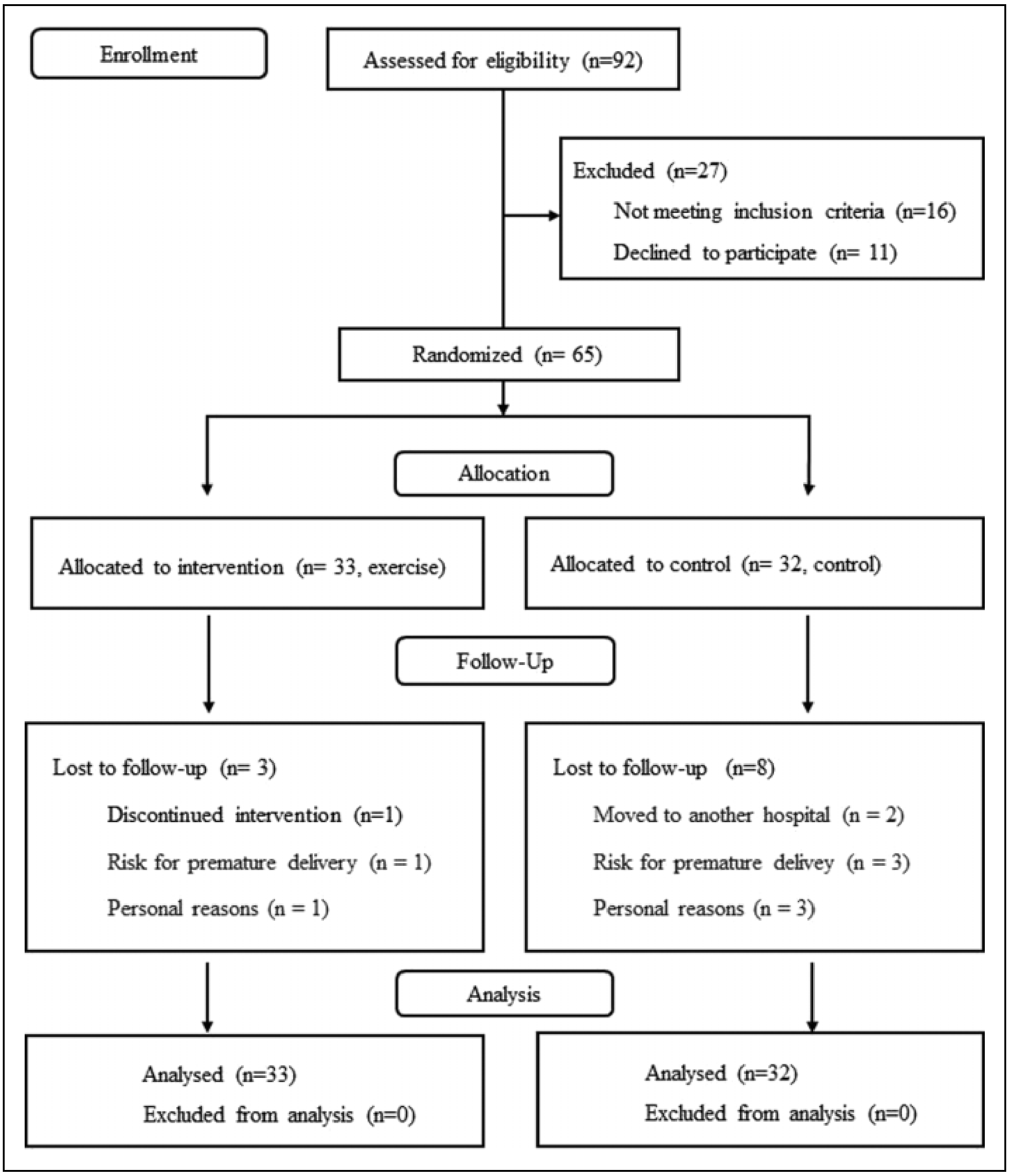

Figure 1. Flow chart of study participants.

main finding of our study was that supervised, moderate exercise training performed throughout pregnancy (85 training sessions in total) does not negatively affect PW. Furthermore, the overall health status of the newborn was unaffected as reflected by the results of the widely used Apgar score.

An additional novelty of our study was that the exercise program integrated light resistance, toning, aerobic dance, and pelvic floor exercises, which was easily incorporated into a structured exercise regime for pregnant women. The variety of activities of this program focuses its effects on

Table 1. Maternal Characteristics.

Variables	EG ($N = 33$)	CG ($N = 32$)	p
Age (years)	33.1 ± 3	33.8 ± 2	.45
BMI	24.1 ± 3.9	24.4 ± 6	.80
Prepregnancy BMI (*n*/%)			
<18	2/6.1	1/3.1	.90
18–24.9	22/66.7	22/68.8	
25/29.9	5/15.2	6/18.8	
>30	4/12.1	3/9.4	
Parity (*n*/%)			
No previous gestation	23/69.7	19/59.4	.38
One or more previous gestations	10/30.3	13/40.6	
Smoking during pregnancy (*n*/%)			
No	28/84.8	28/87.5	.75
Yes	5/15.2	4/12.5	
Occupation (*n*/%)			
Housewife	11/33.3	10/31.2	.93
Sedentary job	9/27.3	8/25	
Active job	13/39.4	14/43.8	
Previous miscarriage (*n*/%)			
None	25/75.8	26/81.2	.80
One	6/18.2	5/15.6	
Two or more	2/6.1	1/3.1	

Note. Data are expressed as the mean ± standard deviation unless otherwise indicated. We analyzed continuous and nominal data with Student's *t* test for unpaired data and the χ^2 test, respectively. BMI = body mass index at the beginning of the study; EG = exercise group; CG = control group.

the modifications that the pregnancy process generates and decreasing the discomforts of pregnant women. It seems that this program was highly liked by the pregnant women as indicated by the high rate of adherence. To our knowledge, this is the first controlled, randomized trial that objectively and specifically shows no cause–effect relationship between supervised, regular exercise and PW.

The main interest of this study was on the influence of exercise on PW because the placenta plays a major role in fetal nutrition and fetal growth, as nutrients from the maternal circulation need to be transported (across the placenta) to reach the fetal circulation environment (Baumann, Deborde, & Illsley, 2002).

In an observational and prospective study, Salafia et al. investigated seven maternal characteristics (age, height, weight, parity, socioeconomic

Table 2. Primary and Secondary Outcomes of the Study Groups.

	All (n = 65)		
Variable	EG (n = 33)	CG (n = 32)	p
Placental weight (g)	495.4 ± 150	493.2 ± 119.6	.95
Placental weight categories			
Low (n/%)	4/12.1	5/15.7	.57
Normal (n/%)	26/78.8	26/81.2	
High (n/%)	3/9.1	1/3.1	
Ratio PW:BW	0.157 ± 0.03	0.158 ± 0.03	.96
MWG (kg)	10.9 ± 2.7	11.8 ± 4.8	.43
Excessive MWG (n/%)	4/12.1	8/25	.18
Categories of PW in adequate MWG			
Low PW (n/%)	4/13.8	5/22	.68
Normal PW (n/%)	23/79.3	16/72.7	
High PW (n/%)	2/6.9	1/4.5	
Categories of PW in excessive MWG			
Normal PW (n/%)	3/75	10/100	.10
High PW (n/%)	1/25	0/0	
Gestational age (days)	277.9 ± 12.5	276.9 ± 11.2	.77
Preterm delivery, <37 week (n/%)	2/6.1	2/9.4	.61
Type of delivery (n/%)			.77
Normal	18/54.5	19/59.4	
Instrumental	10/30.3	10/31.2	
Cesarean	5/15.2	3/9.4	
Newborn			
BW (g)	3,117.6 ± 476	3,122.9 ± 453	.96
BW categories			
Low <2,500 (n/%)	3/9.2	4/12.5	.53
Adequate 2,500–4,000 (n/%)	29/88	26/81.4	
Macrosomia >4,000 (n/%)	1/2.8	2/6.1	
Apgar score 1 min	8.6 ± 0.4	8.7 ± 1.2	.47
Apgar score 5 min	9.6 ± 0.8	9.7 ± 0.4	.40

Note. The data are expressed as the mean ± standard deviation unless otherwise indicated. We analyzed continuous and nominal data with Student's t test for unpaired data and the χ^2 test, respectively. EG = exercise group; CG = control group; PW = placental weight; BW = birth weight; MWG = maternal weight gain.

status, smoking, and race) and determined whether their known associations with BW were mediated by placental markers. The authors reported that all of the maternal characteristics except smoking were mediated by placental characteristics (Salafia et al., 2008).

Other external factors, such as maternal life stress (Tegethoff, Greene, Olsen, Meyer, & Meinlschmidt, 2010) or prepregnancy nutritional status and maternal diet during pregnancy (Thornburg et al., 2010), have been associated with PW.

In a prospective longitudinal study, Roland et al. (2014) found that maternal factors known to influence fetal growth and newborn outcomes (BW and neonatal body composition), such as maternal BMI, gestational weight gain, or fasting glucose, are determinants of PW.

In an experimental study (in which the authors did not clarify whether it was an RCT), Ramirez-Velez et al. (2013) reported that during the second half of pregnancy, regular exercise increased endothelial nitric oxide synthases expression and nitric oxide production and decreased reactive oxygen species generation in the human placenta. The authors expressed that increased endothelial shear stress may contribute to the beneficial effects of exercise on the vascular and antioxidant system and, in turn, reduce the risk of preeclampsia, diabetes, or hypertension during pregnancy (Ramírez-Vélez, Bustamante, Czerniczyniec, Aguilar de Plata, & Lores-Arnaiz, 2013).

The known influence of exercise on maternal and fetal outcomes (Barakat et al., 2016; Perales et al., 2016; Ruiz et al., 2013) suggests that physical exercise during pregnancy would influence the weight of the placenta. In fact, the circulatory changes caused by exercise (i.e., redistribution) may disrupt the normal flow of maternal blood to the uteroplacental area (Mottola, 2013; Veille, 1996) and thereby alter the normal development of the placenta. However, our results regarding PW and PW:BW ratio do not support the idea of this disruption (or other effects) caused in theory by physical exercise and therefore informed the nonconfirmation of our initial hypothesis. This could be due to the disruptions mentioned above being generated by higher intensity exercise. Clapp, Kim, Burciu, & Lopez (2000) suggested that exercise performed at moderate to high intensity influences fetal–placental growth and the effects depend on the frequency, duration, and intensity of exercise sessions; moreover, the different types of maternal carbohydrate intake and the relative amount of exercise (in late pregnancy) influence late fetal growth (Clapp, 2003). In our study, the exercise was more of a moderate intensity throughout pregnancy, rather than high intensity, and this may have allowed the placenta to adapt to the exercise and thus no effects were seen that disrupted fetal or placental growth. Recent scientific evidence supports the idea of exercise of moderate intensity throughout pregnancy to achieve maternal and fetal benefits without associated risks (Perales, Artal, & Lucia, 2017).

The main limitation of the present study was that we were unable to measure factors that could influence the primary outcome, such as nutritional status, daily time in standing, or PW of previous deliveries (if any). We conclude that a regular, supervised exercise program throughout pregnancy does not affect the PW of healthy pregnant women.

We believe that there exists a significant gap in this scientific topic. Our results supplement an important portion of the scientific literature that studies the relationship between exercise and pregnancy. We believe that more clinical trials with large samples sizes are needed by examining other factors such as psychic, emotional, or nutritional. In addition, it would be interesting to study the relationship between the PW and the relationship between the PW and "child growth."

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A la vista de los resultados de las cuatro publicaciones, podemos constatar que ni el bienestar fetal ni el materno, parecen verse afectados por la realización de un programa de ejercicio físico de intensidad moderada supervisado durante la gestación.

Peso materno y fetal

Parece demostrado que la ganancia ponderal materna durante la gestación tiene un impacto sobre la gestación y sobre el futuro recién nacido(5,10,12–20,37). Meta-análisis anteriores demostraron que el ejercicio físico regular, realizado tres veces por semana durante alrededor de una hora, de intensidad moderada durante la gestación previene de la ganancia ponderal excesiva(153–155). Sin embargo, en nuestro estudio, **no hemos encontrado diferencias en la ganancia global de peso al final de la gestación entre los grupos**, aunque sí que se puede observar una tendencia a una menor ganancia ponderal en el grupo intervención. En las diferentes publicaciones, el efecto del ejercicio sobre el peso materno parece ser mayor en las gestantes obesas o con sobrepeso al inicio de la gestación. Sin embargo, no hemos podido hacer un análisis por subgrupos según el IMC inicial debido al tamaño muestral reducido(109,109–116).

Por otro lado, hemos detectado que **las gestantes que siguen un programa de ejercicio físico de intensidad moderada a lo largo de la gestación pierden más peso tras el parto**, lo que ayudaría a evitar la obesidad o sobrepeso, ambos frecuentes tras el parto y por lo tanto disminuiría sus consecuencias a largo plazo(109–116).

Cuando analizamos el **peso fetal al nacimiento no encontramos diferencias entre los grupos**. No hemos encontrado un aumento en el número de fetos con bajo peso al nacimiento (pesos al nacimiento inferiores al percentil 10) ni diferencias en fetos grandes para la edad gestacional (pesos al nacimiento mayores de 4Kg o superiores al percentil 90). En la literatura, sin embargo, sí parece observarse una disminución del riesgo de tener fetos grandes para la edad gestacional cuando se realiza ejercicio durante la gestación, con una OR de 0.69(75), sin que aumente el riesgo de tener fetos pequeños para la edad gestacional(76,156).

Edad gestacional al parto y resultados perinatales

La edad gestacional al parto ha resultado ser la misma en los dos grupos estudiados y no ha aumentado a tasa de parto pretérmino antes de la semana 37, lo que apoya lo ya descrito por la literatura(32,45,46), es decir, que **la realización de un programa de ejercicio de intensidad moderada supervisado durante la gestación no aumenta el riesgo de parto pretérmino**.

En relación con **la vía del parto o necesidad de inducción, no hemos encontrado diferencias**. La evidencia sobre este tema es controvertida. Estudios recientes sugieren que la realización de ejercicio regular durante la gestación podría reducir el riesgo de cesárea(157–161), aunque otros no han encontrado este efecto(159,162,163). También se ha descrito que el ejercicio podría favorecer el inicio espontáneo del parto(164,165), aunque hay resultados controvertidos(163,166,167).

El peso placentario tampoco parece verse afectado por la práctica del ejercicio físico supervisado de intensidad moderada durante la gestación. Es sabido que la placenta tiene un papel crucial en la nutrición y el crecimiento fetal(168,169). Ramirez-Velez et al.(170) describieron que, durante la segunda mitad del embarazo, la realización de ejercicio aumentaba la síntesis del óxido nítrico endotelial y disminuía los radicales libres en la placenta humana. Esto podría contribuir en una mejora del sistema vascular y antioxidante de la placenta, disminuyendo el riesgo de preeclampsia, diabetes o hipertensión durante la gestación. Por otro lado, los cambios a nivel de la circulación materna durante el ejercicio podrían influir de manera negativa en el flujo sanguíneo a la placenta condicionando el desarrollo placentario(171,172). Sin embargo, en nuestro estudio no encontramos diferencias a este nivel, lo que podría deberse a la intensidad del ejercicio, siendo más probable que esa disrupción en el flujo hacia la placenta aparezca con ejercicios de intensidad vigoroso.

Muchos estudios utilizan el test de Apgar y el pH de cordón umbilical al parto para valorar el estado bienestar fetal y evaluar los efectos adversos de las intervenciones durante la gestación(47,48,173). El pH del cordón umbilical nos indica el estado de oxigenación fetal en el momento del parto, y el test de Apgar la capacidad fetal a adaptarse a la vida extrauterina. Para que el feto tenga una buena oxigenación es necesario que la placentación y la circulación uteroplacentaria sea adecuada en todo momento (174,175). Una alteración a nivel placentario ya sea de manera aguda durante el parto (por ejemplo, por un exceso de contracciones, infecciones, un *abruptio placentae)* o crónico (una insuficiencia placentaria), comprometerán la oxigenación fetal y por lo tanto podrán alterar el pH arterial fetal, volviéndolo acidótico. La acidosis fetal al nacimiento se ha puesto en relación con la aparición de malos resultados fetales a largo plazo (parálisis cerebral, muerte fetal, etc.)[176–179]. El Apgar es un score desarrollado para intentar valorar la adaptación del neonato a la vida extrauterina[180] y una baja puntuación, especialmente a los 5 minutos de vida, se ha puesto en relación con efectos deletéreos a largo y corto plazo[181,182]. De todas maneras, ambos parámetros, el test de Apgar y el pH de cordón, están muy influenciados por los acontecimientos propios del parto, con lo que es poco probable que intervenciones sutiles acontecidas durante la gestación puedan influir en ellos.

En nuestro estudio **no hemos encontrado diferencias entre los grupos ni en el pH arterial al parto, ni en la incidencia de Apgar <6 a los 5 minutos**. Tampoco hemos encontrado diferencias significativas en cuando a la **proporción de neonatos que requieren ingreso en la unidad de cuidados intensivos**. Todo esto hace pensar que el efecto del ejercicio no afecta a nivel de oxigenación fetal, es decir, que su práctica de manera regular durante la gestación no condiciona unos cambios a nivel placentario tales que puedan condicionar la aparición de una hipoxia durante el parto.

Cambios fisiológicos maternos

La glucosa es esencial para el buen desarrollo fetal[127], y el ejercicio aumenta la captación de la glucosa por los músculos y, por lo tanto, podría producir una hipoglucemia que en la madre gestante podría condicionar el bienestar fetal. En nuestro estudio **no hemos encontrado diferencias en los niveles de glucosa basal en ayunas en ninguna de las analíticas realizadas a lo largo de la gestación, ni tras la sobrecarga oral de glucosa entre los grupos**. Sin embargo, en estudios anteriores[129,130] sí que se encontraron diferencias en los niveles de glucosa tras el test de sobrecarga oral de glucosa. La diferencia entre los estudios puede deberse a que en nuestro estudio esta prueba se realizaba sin ayunas, mientras que en los otros dos estudios las gestantes acudían en ayunas. En algunos estudios se ha postulado que el ejercicio podría ayudar a un mejor control de la glucosa en gestantes diabéticas[132–134]. Estos datos nos hacen postular que, posiblemente el ejercicio ayude a mantener los niveles glucémicos dentro de los límites normales sin que se llegue a la hipoglucemia pese al estrés. De cualquier manera, nuevos estudios deben llevarse a cabo para poder dilucidar el metabolismo de la glucosa en estas gestantes.

La influencia del ejercicio sobre el metabolismo hepático de la gestante no se ha estudiado hasta la fecha. En población general no gestante se sabe que el ejercicio aumenta los niveles de la enzima AST y su actividad(135,136). En nuestro estudio **no encontramos diferencias en los niveles de las enzimas hepáticas AST y Alanina aminotransferasa (ALT) entre los grupos**, aunque el tamaño muestral puede ser una limitación importante a la hora de detectar diferencias.

A nivel renal, en nuestro estudio no hemos encontrado diferencias entre los grupos, de manera consistente con lo descrito por la literatura(128). Es cierto que es controvertido si la excreción de urea nitrogenada podría verse afectada por la realización de ejercicio(137), pero en nuestro estudio no pudimos realizar el análisis de ese metabolito.

Cambios cardiovasculares maternos

Se han descrito algunos cambios cardiovasculares en gestantes que realizaron ejercicio moderado supervisado a lo largo de la gestación(121,122). Dentro de estos, se ha constatado una disminución de la frecuencia cardiaca basal, así como una menor tensión sistólica y diastólica(123,124), lo que hablaría de una adaptación positiva del sistema cardiovascular materno. El ejercicio físico parece reducir el estrés oxidativo, mejorar la función endotelial y mejorar la respuesta inmune e inflamatoria, así como mejorar el gasto cardiaco(125,126). En nuestro estudio no solo no hemos encontrado este efecto, sino que además hemos encontrado una tensión sistólica mayor en el GI a las 27^{+0}-28^{+6} semanas de gestación, dentro de los parámetros normales para la gestación. Este hallazgo no parece consistente con la fisiopatología normal de la gestación ni de la realización de ejercicio, con lo que debemos ponerlo en duda y achacarlo al efecto de la realización de múltiples comparaciones. Sin embargo, nuevos estudios a este respecto deberían realizarse para poder descartarlo definitivamente.

Función cardiaca Fetal

Hoy en día se cree que las enfermedades cardiovasculares del adulto tienen una fase latente o inicial en la vida intrauterina[183–186]. Esto se ha estudiado especialmente en fetos expuestos a un ambiente intrauterino poco favorable[19,49,50,139–141], y se han visto una serie de modificaciones cardiovasculares que pueden condicionar la salud cardiovascular durante la infancia y la etapa adulta.

En nuestro estudio **la función cardiaca fetal no parece verse afectada por el ejercicio**. Parece observarse una tendencia en el GI a tener un IP a nivel del Ductus Arterioso (DA) mayor que en el GC, lo que podría prevenir del cierre precoz del mismo durante la gestación. Posiblemente este hecho sea reflejo del mayor estrés al que se expone el feto al inicio de la realización del ejercicio físico de su madre y que el feto compensa inicialmente aumentando el IP del DA. Por otro lado, se observa una mayor fracción de Eyección (FE) cardiaca fetal en el GI a las 36 semanas y este hecho es la primera vez que se ha estudiado. Posiblemente sea reflejo de esa adaptación paulatina al ejercicio del feto. Los cambios observados en el DA y en la FE, pueden estar reflejando la adaptación fetal al estrés, aunque el significado real de los hallazgos realizados a este nivel se debe comprobar y dilucidar en futuros estudios.

Flujo vascular fetomaterno

Cuando se ha estudiado **los flujos vasculares fetomaternos mediante ecografía Doppler, no se ha objetivado ningún tipo de deterioro que pueda poner en riesgo el bienestar fetal**. El flujo vascular fetomaterno es similar en ambos grupos en todas las edades gestacionales estudiadas. Lo que sí parece evidenciarse es una adaptación fetal al ejercicio, por medio de una disminución del IP normalizado mediante z-score de la Arteria Umbilical (Au) a lo largo de la gestación que prepararía al feto para una mejor respuesta al estrés. Dado que el IP de la Au, refleja la oxigenación y perfusión placentaria, podemos teorizar que inicialmente se eleva el IP Au como respuesta a una hipoperfusión durante la realización del ejercicio. Según avanza la gestación el sistema cardiovascular materno mejora con la realización el ejercicio y por lo tanto se mejora la perfusión y oxigenación placentaria, disminuyendo el IP Au. Existen tres ensayos aleatorizados que estudian el impacto del ejercicio realizado de manera crónica durante la gestación[(65–67)] En ninguno de ellos, se encuentran diferencias significativas en situación basal. Sin embargo, uno[(67)] describe una disminución del IP Au en el Doppler de las gestantes del GI tras exponer a las gestantes a las 34 semanas a un *cycle-ergometer* test en el grupo ejercicio. Esto pondría de manifiesto la mejor adaptación al estrés agudo de las gestantes que realizan ejercicio moderado supervisado a lo largo de la gestación, pero no en el ejercicio físico realizado de forma crónica, como se ha demostrado en el presente estudio.

CONCLUSIONES

En mujeres embarazadas de bajo riesgo, un programa regular de ejercicio físico de intensidad moderada supervisado:

1. No altera el bienestar ni materno ni fetal.
2. Aumenta la pérdida de peso materno a las 6 semanas del parto
3. No deteriora el flujo vascular fetomaterno
4. Podría tener una asociación beneficiosa con el desarrollo cardiovascular fetal.
5. No afecta al volumen placentario
6. No altera los cambios fisiológicos normales que ocurren durante el embarazo

Por lo tanto:

la práctica de ejercicio físico durante el embarazo es segura para el feto, ya que se conserva la perfusión placentaria y la oxigenación fetal.

Se necesitan grandes estudios prospectivos para dilucidar la relación entre el ejercicio durante el embarazo y todas estas variables estudiadas, a corto y largo plazo, así como estudios sobre el impacto tanto a nivel clínico como económico de la implementación poblacional de programas de ejercicio físico controlado de intensidad moderada durante todo el embarazo en gestantes de bajo riesgo.

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