PROGRAMA DE DOCTORADO DE INVESTIGACIÓN EN BIOMEDICINA

TESIS DOCTORAL POR COMPENDIO DE PUBLICACIONES

LA CIRUGÍA EN EL PACIENTE ANCIANO. IMPACTO DE LA FRAGILIDAD EN SUS RESULTADOS A CORTO Y LARGO PLAZO.

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En Las Palmas de Gran Canaria, a 28 de abril de 2021.

AGRADECIMIENTOS

A Joaquín Marchena Gómez, Director de esta tesis, Jefe de Servicio y pilar fundamental en mi formación quirúrgica e investigadora. Sus ideas innovadoras, su rigor científico y su interés por la atención adecuada al paciente geriátrico, han hecho posible este proyecto. Le agradezco su eterna paciencia y la confianza depositada en mí para desarrollar esta línea de investigación. Sin él, esta tesis no hubiese visto la luz.

A Cristina Roque Castellano, codirectora de tesis, compañera de Unidad y un referente quirúrgico en mi desarrollo profesional. Sin su trabajo, esta tesis no sería realidad. Te estaré eternamente agradecido.

A mi familia, por ser mis grandes apoyos y por recordarme que con esfuerzo todo es posible.

A Sara Almeida González, por acompañarme en todo el proceso, sentirlo como suyo y darme fuerzas cuando más cansado estaba.

Al Roberto Fariña Castro, por su ayuda y por hacerme partícipe de sus investigaciones en este campo.

A mis compañeros de Servicio, por su apoyo.

Y, en especial, a cada uno de los pacientes y familiares que comprendieron la relevancia del proyecto y accedieron a participar en él. Con cada entrevista me permitieron conocer quienes eran, cómo había sido su vida, me entretuvieron con sus experiencias y, sobre todo, me enseñaron a comprender sus necesidades, lo cual no hubiese aprendido de otra manera.

La cirugía en el paciente anciano. Impacto de la fragilidad en sus resultados a corto y largo plazo.

Índice

INTRODUCCIÓN

Según datos de la Organización Mundial de la Salud (OMS)[1], el envejecimiento de la población, tanto en los países desarrollados como en los países en desarrollo, es un indicador de la mejora de la salud mundial. En las últimas décadas, la expectativa de vida de la población global ha aumentado considerablemente, viviendo así una evidente inversión de la pirámide poblacional. Por primera vez en la historia, la mayor parte de la población mundial tiene una edad igual o superior a los 60 años.

Hoy en día, existen 125 millones de personas en el mundo con edades superiores a los 80 años. Se estima que en el año 2050, solamente en China, habrá un número casi igual de personas mayores de 80 años (120 millones), y 434 millones de personas de este rango de edad en todo el mundo. Para ese mismo año, el 16% de la población mundial tendrá más de 65 años, suponiendo esto un incremento significativo de las demandas de atención sanitaria por este grupo de edad[1].

En el caso concreto de España, el Instituto Nacional de Estadística recoge un incremento del 3,03% de la población con 70 años o más en los últimos 20 años[2].

De forma general, un mayor envejecimiento de la población mundial, acarrea un mayor volumen de pacientes con enfermedades o trastornos crónicos. Una gran proporción de estos trastornos, como pueden ser el cáncer, la arteriopatía, los trastornos visuales o la patología osteoarticular, cuentan con la opción quirúrgica en su plan terapéutico[3–5]. En la actualidad, son más de 4 millones de intervenciones quirúrgicas las que se realizan en Estados Unidos en adultos mayores, viviendo un incremento paralelo de la morbimortalidad operatoria asociada a la edad[6].

En lo relativo a la patología oncológica, el Cáncer Colorrectal (CCR) es la tercera neoplasia más frecuente de forma global, y la cuarta causa más común de muertes relacionadas con el cáncer[7]. En todo el mundo, se registran alrededor de 1,4 millones de casos cada año, atribuyéndose alrededor de 0,7 millones de muertes al CCR. Además, presenta una incidencia creciente en la actualidad. El tratamiento de elección se ve condicionado por diferentes factores, incluyendo la clínica de presentación, la localización del tumor, su estadiaje y las condiciones basales del paciente. El esquema de tratamiento actual del cáncer de colon se basa en la cirugía en los estadios I y II; la cirugía junto con quimioterapia adyuvante en el estadio III; y la quimioterapia neoadyuvante con posibilidad de cirugía de rescate en casos de cáncer de colon metastásico. El cáncer de recto incluye la cirugía directa en los estadios I; o la combinación de radioterapia o quimiorradioterapia y cirugía posterior, con quimioterapia adyuvante en casos de estadios II y III. Según datos del *National Cancer Intelligence Network* (NCIN), aproximadamente el 60% de los pacientes con CCR son mayores de 70 años en el momento del diagnóstico, siendo el 43% de ellos mayores de 75 años[8]. A su vez, se espera que estas proporciones continúen incrementándose en un futuro cercano.

Conforme la persona envejece, se produce un deterioro fisiológico de todos los sistemas orgánicos, variando su magnitud entre individuos y dependiendo del órgano afecto. Si bien en un estado de reposo esta merma fisiológica puede tener mínimas consecuencias funcionales, en un estado de estrés metabólico, como podría ser una intervención quirúrgica, se disponen de menos recursos para hacer frente a dicha situación y la función global puede empeorar notablemente.

Durante la preparación de una cirugía en un adulto mayor, hay dos cuestiones de gran importancia que deben ser tenidas en cuenta. En primer lugar, la presentación y evolución natural de la enfermedad en este grupo de pacientes puede no ser igual que en el adulto joven, de forma que las opciones de tratamiento deben considerar estas diferencias. En segundo lugar, el paciente anciano es diferente desde el punto de vista fisiológico y psicológico respecto al adulto joven.

Decidir si un paciente mayor puede tolerar un determinado procedimiento o no, así como estimar cual será su calidad de vida posterior, ha sido tradicionalmente un procedimiento subjetivo y condicionado en la mayoría de las ocasiones por la propia experiencia previa del cirujano. Hasta ahora, la edad y la comorbilidad han sido considerados los factores discriminativos principales para determinar si un adulto mayor podía ser intervenido, asociándolas con un efecto negativo en el pronóstico a corto y medio plazo. De esta forma, ha habido cierta reticencia a someter a estos pacientes a un procedimiento quirúrgico, y algunos grupos incluso consideraron que ningún tratamiento era la mejor opción terapéutica en esta población[9]. Este conjunto de decisiones se lleva aún más al extremo en el caso de pacientes octogenarios y nonagenarios, a pesar de conocer que las mejoras en el manejo perioperatorio y el desarrollo de la cirugía mínimamente invasiva han proporcionado grandes beneficios postoperatorios en esos grupos de edades extremas[10].

Hoy en día, el papel pronóstico que juegan factores como la fragilidad o el estado cognitivo o funcional, han atraído mayor atención[11]. Estas últimas variables permiten identificar a aquellos casos con alta probabilidad de desarrollar complicaciones adversas tras un procedimiento, prevenir estos acontecimientos y facilitar la toma de decisiones

por parte del paciente y de su familia; habiendo demostrado asímismo ser predictores independientes para el desarrollo de complicaciones postoperatorias en pacientes sometidos a procedimientos gastrointestinales mayores, osteoarticulares o cardiovasculares, entre otros[12–17].

Si bien no existe una definición clara para el concepto “fragilidad”, clásicamente se ha considerado como un síndrome multifactorial caracterizado por un estado de vulnerabilidad y limitación de los mecanismos compensadores ante factores estresantes, condicionando una predisposición para padecer efectos adversos derivados de una intervención[18]. Los adultos mayores frágiles toleran y se adaptan peor que los jóvenes a los factores estresantes, las enfermedades agudas, los traumatismos o las intervenciones quirúrgicas o médicas. Esta mayor vulnerabilidad contribuye a un mayor riesgo de caídas, complicaciones tras un procedimiento, delirio, institucionalización, discapacidad y muerte[19]. Por lo general, este concepto ha sido aplicado previamente a pacientes no quirúrgicos, existiendo aún varias dudas por resolver respecto a su uso en pacientes quirúrgicos[20,21].

La prevalencia de la fragilidad varía en función de la herramienta utilizada para su determinación, así como con la población estudiada. Según datos presentados en un estudio nacional, se estima que un 10-20% de la población mayor de 65 años es frágil, siendo esta tasa superior al 50% en octogenarios y aún mayor en nonagenarios[22]. En Estados Unidos, la prevalencia de fragilidad varía de 4 a 16% en pacientes de 65 años o más, alcanzando hasta un 43% en adultos mayores con cáncer[21]. En el caso concreto de los nonagenarios, un estudio americano estima una prevalencia de fragilidad del 24% para aquellos pacientes con edades de 90-94 años, elevándose hasta el 39,5% en

aquellos con edades superiores a 95 años[23].

A la vista de los resultados de un reciente metaanálisis, la fragilidad preoperatoria implica un riesgo 2,77 veces mayor de mortalidad a 30 días, así como un riesgo 1,99 veces mayor de fallecer un año después de una intervención quirúrgica[24]. Estos resultados son respaldados por los de otras dos revisiones sistemáticas y metaanálisis recién publicados con un objetivo similar, asociándose la fragilidad con un aumento de la mortalidad, las complicaciones postoperatorias y la estancia hospitalaria[25,26]. No obstante, aunque el Colegio Americano de Cirugía recomienda la evaluación sistemática de la fragilidad en el entorno preoperatorio, la definición y los criterios de medición de la fragilidad previa a la intervención siguen sin estar claros[27,28].

Han sido muchas las herramientas que se han desarrollado para la identificación de la fragilidad en el anciano[29,30], siendo su utilidad muy variable entre las diferentes poblaciones de pacientes, las indicaciones de cirugía y los procedimientos realizados[31,32]. Por otro lado, la mayoría de las herramientas propuestas para su determinación se basan en la edad cronológica, las comorbilidades o derivan de la obtención de información subjetiva aportada por el enfermo, complicando notablemente la toma de decisiones quirúrgicas en este grupo de pacientes. En este sentido, una revisión sistemática publicada en 2016, identificó hasta 67 escalas de fragilidad, encontrándose estos scores compuestos casi por las mismas variables y con alta concordancia entre ellos[33,34]. En la práctica clínica actual, el establecimiento de una definición consensuada de fragilidad se ha visto mermado en gran parte por esta abrumadora proliferación de herramientas de determinación, con diferentes bases

conceptuales y que a menudo no logran diferenciar entre dependencia, comorbilidad y fragilidad, que, si bien son conceptos distintos, se encuentran íntimamente relacionados entre sí. Finalmente, y teniendo en cuenta lo previamente expuesto, podemos entender que no existe en la actualidad una medida *gold standard* para determinar la fragilidad.

Las escalas más comúnmente aceptadas para definir la fragilidad son:

- Canadian Study of Health and Aging (CSHA) Clinical Frailty Scale (CFS) (CSHA-CFS)[35]. Es un test simple, fiable y validado. Fue propuesto por Rockwood et al. como una nueva herramienta capaz de relacionar la fragilidad con la mortalidad o la necesidad de atención institucional. Esta escala de 7 puntos varía desde 1 punto (muy en forma) a 7 puntos (muy frágil) utilizando datos clínicos obtenidos a partir de una breve entrevista al paciente.

- Fried Frailty Tool o Frailty Phenotype[36]. Fue validada en el Cardiovascular Health Study (CHS), que involucró a más de 5000 pacientes de 65 años o mayores. Requiere de la participación del paciente y de un equipo especializado para determinar la fuerza de agarre y la velocidad al caminar.

- 11-item mFI Modified Frailty Index (11-mFI) y 5-item mFI Modified Frailty Index (5-mFI)[37–39]. Son dos versiones diferentes del Modified Frailty Index propuesto por el Programa Nacional de Mejora de la Calidad Quirúrgica del Colegio Americano de Cirujanos (ACS-NSQIP). Para su determinación recoge antecedentes o comorbilidades concomitantes.

- Groningen Frailty Indicator[40,41]. Es una herramienta de evaluación que incluye cuatro preguntas sobre movilidad, cuatro sobre cuestiones psicosociales, una sobre aptitud física, visión, audición, peso, polifarmacia y cognición.

Para algunos autores, la comorbilidad debe valorarse aparte de la fragilidad. Pueden existir pacientes frágiles sin comorbilidad y pacientes con comorbilidad sin fragilidad. En un estudio de Fried et al.[36], el 25% de los pacientes frágiles no padecían comorbilidad o discapacidad alguna. Para valorar la comorbilidad se han definido múltiples escalas. Las dos escalas más comúnmente utilizadas en el ámbito quirúrgico son:

- Clasificación ASA (American Society of Anesthesiologists)[42]. Esta escala se desarrolló para ofrecer una categorización simple del estado fisiológico de un paciente, que podría ser útil para predecir el riesgo operatorio. Si bien se trata de una escala de riesgo anestésico, su determinación se basa en la comorbilidad del paciente.

- El Índice de Comorbilidad de Charlson[43]. Incluye un total de 19 condiciones médicas, a las cuales se les asigna un valor de 1, 2, 3 o 6 puntos basándose en la magnitud del riesgo relativo asociado a cada una de ellas, y obteniendo una puntuación final que oscila 0 y 37 puntos. Probablemente, este es el índice más utilizado para la determinación de comorbilidad.

Entendemos por Valoración Geriátrica Integral (VGI) aquel proceso diagnóstico-terapéutico dinámico, estructurado, multidimensional y multidisciplinario, que se lleva a cabo para determinar los problemas médicos, mentales y funcionales de las personas

mayores frágiles[44]. Abarca cuatro esferas: clínica, mental, funcional y social, configurando al final del proceso la imagen real del adulto mayor. Se ha considerado como la forma más acertada de estimar la edad biológica de un paciente, dejando de lado la edad cronológica. Los objetivos principales de la VGI serían: mejorar la función física y psicológica, optimizar el uso de medicamentos, disminuir los ingresos en centros de cuidados intermedios y la estancia hospitalaria, disminuir el riesgo de mortalidad y mejorar la satisfacción del paciente. Mediante esta estrategia se puede desarrollar un plan coordinado e integrado de tratamiento y seguimiento, de forma que se consigue un mayor grado de independencia y una mejor calidad de vida, así como la optimización de los recursos y la disminución de costes sanitarios, especialmente en el preoperatorio de pacientes mayores oncológicos[45]. Las principales áreas personales que deben evaluarse durante la VGI son: la capacidad funcional, la capacidad instrumental, el riesgo de caídas, el estado cognitivo, el estado anímico, el tratamiento farmacológico basal, el apoyo social y el estado nutricional. Nuevamente, al igual que ocurre en la determinación de fragilidad, nos encontramos con una gran cantidad de escalas de valoración para cada una de las esferas. Algunas de las más utilizadas son:

- Índice de Barthel[46]. Evalúa las actividades básicas de la vida diaria: comer, lavarse, vestirse, arreglarse, ir al retrete, continencia defecatoria, continencia miccional, transferencia cama-sillón, deambular y capacidad de subir y bajar un piso. La puntuación total oscila entre 0 (dependencia completa) y 100 (máxima independencia). Sus resultados pueden ser agrupados para una mejor estratificación, por ejemplo: dependencia (<80 puntos) o independencia (80-100 puntos).

- Índice de Actividades de la Vida Diaria (KATZ)[47]. Similar al Índice de Barthel en sus áreas de valoración, los pacientes son clasificados desde la letra A (máxima independencia) a la G (máxima dependencia).

- Índice de Lawton y Brody[48]. Valora las actividades instrumentales de la vida diaria. Este índice determina la capacidad de la persona de realizar diferentes actividades instrumentales necesarias para llevar una vida independiente: usar el teléfono, comprar, preparar la comida, cuidar la casa, lavar la ropa, utilizar el dinero, usar medios de transporte y controlar su medicación. Su puntuación varía desde 0 (dependiente) a 8 puntos (independiente) para las mujeres, y de 0 a 5 puntos para los hombres.

- Test "Timed Up and Go"[49]. Mide el tiempo en segundos que tarda el paciente en levantarse de una silla, andar 3 metros, girar, volver y sentarse. Tiempos de 15 segundos o más se correlacionan fuertemente con la fragilidad y el aumento de las complicaciones posoperatorias y la mortalidad a un año[50].

- Cuestionario de Estado Mental Portátil de Pfeiffer[51]. Desarrollado en 1.975, examina la memoria a corto y largo plazo, la orientación, información sobre hechos cotidianos y la capacidad de cálculo. Este cuestionario breve (10 ítems), proporciona una estimación del estado cognitivo de un paciente según el número de respuestas incorrectas a preguntas básicas, con valores que van de 0-1 (sin deterioro) hasta 9-10 (deterioro más grave).

- Índice de Masa Corporal (IMC) y el cuestionario Mini Nutritional Assessment Short Form (MNA-SF)[52]. Se utilizan para evaluar el estado nutricional del

paciente. El MNA-SF es una herramienta de evaluación de 6 elementos basada en el IMC del paciente, un cuestionario dietético y una evaluación subjetiva. La puntuación máxima es de 14 puntos. El riesgo de desnutrición aumenta al disminuir las puntuaciones.

En el caso concreto de los adultos mayores intervenidos por CCR, algunos estudios sugieren que la fragilidad es un predictor eficaz para el desarrollo de complicaciones postoperatorias graves[37,38,44,53,54]. En este sentido, la Sociedad Internacional de Oncología Geriátrica recomienda el uso de la VGI para orientar el desarrollo de un plan de tratamiento oncológico en pacientes mayores con cáncer, incluidos aquellos que necesitan someterse a cirugía[45]. Por lo tanto, la evaluación de la fragilidad en oncología colorrectal parece importante para determinar los riesgos y beneficios operatorios, así como orientar el manejo perioperatorio de esos pacientes. Sin embargo, la relación entre la fragilidad y la supervivencia a largo plazo no se había estudiado bien[39,44], siendo pocos los estudios que han proporcionado un seguimiento de esta población a los 5 años[55]. Además, la variable "fragilidad" en estos informes no suele ajustarse por posibles factores de confusión como la edad, las comorbilidades o el estadio tumoral.

El conocimiento de estos factores en esta población puede ayudarnos a asesorar adecuadamente al paciente y su familia durante el proceso de toma de decisiones preoperatorias. De esta forma, no nos limitamos a rechazar un procedimiento en un paciente mayor frágil, con comorbilidades o en estadios avanzados del cáncer.

Otro punto clave a considerar aquí es la calidad de vida secundaria al deterioro funcional sostenido, especialmente después de la cirugía oncológica[31]. Reducir la

calidad de vida restante en estos pacientes no tendría sentido alguno. Por tanto, la decisión debe tomarse de forma individual con toda la información disponible sobre la supervivencia esperada y la calidad de vida postoperatoria en un intento de evitar el sobretratamiento o el infratratamiento, dos escollos bien conocidos en la oncología geriátrica[55].

No obstante, realizar una valoración geriátrica preoperatoria en el adulto mayor podría convertirse en una labor tediosa y lenta si no se seleccionan las herramientas adecuadas, especialmente si tenemos en cuenta el gran volumen de escalas disponibles y la falta de estandarización en su uso. Este hecho es un gran problema en el entorno quirúrgico, al no disponer en la mayoría de las ocasiones de suficiente tiempo para realizar las entrevistas pertinentes y no ser rentable en algunos pacientes[56]. Por este motivo, se hace necesaria una simplificación de la sistemática que nos permita identificar a los pacientes mayores frágiles de una forma rápida, eficiente y reproducible[57].

Determinar las características preoperatorias de la población anciana sometida a procedimientos quirúrgicos gastrointestinales mayores, especialmente aquellos afectos por cáncer colorrectal debido a su prevalencia, así como cribar la fragilidad preoperatoria mediante una herramienta útil, va a permitir que seamos capaces de identificar de forma objetiva aquellos factores que influyen en el desarrollo de complicaciones postoperatorias y su supervivencia. Esta tarea implicará un mejor asesoramiento respecto al procedimiento que se va a afrontar, una mejora en los cuidados perioperatorios, así como la consecuente reducción de costes sanitarios derivados de una asistencia dirigida a este tipo de población con unas características

particulares[56].

En cuanto a la valoración de los resultados de la cirugía, habitualmente se recurre a las complicaciones postoperatorias y a la mortalidad operatoria. Tal como se comentó con anterioridad, en los ancianos sería recomendable evaluar también el déficit funcional postoperatorio, siendo esto bastante difícil de conseguir en nuestro entorno por falta de medios.

Con respecto a las complicaciones postoperatorias, la tendencia actual es valorar más la gradación de las mismas en función de su gravedad que la simple prevalencia de las mismas. Han sido varias las escalas descritas para ello, siendo las más representativas las siguientes:

- Clasificación de Clavien-Dindo[58]. Se trata de un sistema de gradación de las complicaciones acontecidas en el postoperatorio. El grado I, recoge cualquier desviación en el curso de un postoperatorio normal y que pueda ser fácilmente tratada con fármacos, así como tratamientos que puedan ser llevados a cabo a pie de cama. El grado II incluye el íleo intestinal, las transfusiones de hemoderivados o el uso de nutrición parenteral. El grado III recoge los procedimientos invasivos, ya sean endoscópicos, radiológicos intervencionistas o quirúrgicos, realizados sin anestesia general (grado IIIA) o bajo anestesia general (IIIB). El grado IV incluye complicaciones que precisan de un ingreso en unidades de cuidados intensivos, distinguiendo entre la disfunción de un único órgano (grado IVA) o multiorgánica (grado IVB). Finalmente, la muerte del paciente se categoriza como grado V.

- Comprehensive Complication Index (CCI)[59]. Recoge todas las complicaciones según la clasificación de Clavien-Dindo en una escala numérica ponderada por gravedad. El CCI ha sido recientemente validado para procedimientos quirúrgicos gastrointestinales[60,61], así como económicamente[62]. Los valores del índice oscilan desde 0 puntos (sin incidencias) hasta 100 puntos (fallecimiento).

Por lo tanto, mientras que la Clasificación de Clavien-Dindo se centra solo en la complicación más grave, el CCI incorpora todas las complicaciones y su gravedad.

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JUSTIFICACIÓN

A nivel mundial, la mayor parte de los servicios de salud se han conformado en torno a modelos de atención de procesos agudos que no se correlacionan con los problemas de los adultos mayores. A su vez, este déficit de la atención sanitaria se ve potenciado por la discriminación de cuidados debido al factor edad, así como por el desconocimiento de los cuidados propios de este grupo poblacional. La cirugía moderna debe adaptarse a los cambios poblacionales globales, teniendo en cuenta que el envejecimiento poblacional es un hecho y se produce rápidamente.

En la actualidad, una gran proporción de pacientes intervenidos por un procedimiento gastrointestinal en nuestro medio son considerados mayores. En concreto, el 54% de los pacientes intervenidos de forma electiva por cáncer colorrectal durante el año 2020 en el Hospital Universitario de Gran Canaria Doctor Negrín, tenía una edad igual o mayor de 70 años. Hoy en día es inconcebible seguir asumiendo la edad cronológica como único factor discriminante para la toma de decisiones respecto a un determinado tratamiento en un paciente mayor que precisa una intervención. Conocer las características propias de estos pacientes, la comorbilidad, la fragilidad, así como el desarrollo de complicaciones postoperatorias, ayudaría a ponderar una estimación realista de sus resultados a corto y largo plazo en función de la intervención planificada. Actualmente, existe evidencia suficiente para apoyar una valoración preoperatoria de la fragilidad, identificar al adulto vulnerable, informar apropiadamente acerca de las expectativas del tratamiento, así como actuar apropiadamente para conseguir una recuperación precoz, disminuir la morbimortalidad y los costes socio-sanitarios derivados de su atención.

Determinar el impacto de nuestras intervenciones en el paciente mayor, identificar a aquellos pacientes frágiles que potencialmente pueden desarrollar complicaciones tras la intervención, así como asesorar apropiadamente en la toma de decisiones, han sido las motivaciones principales para el desarrollo de esta línea de investigación.

OBJETIVOS

OBJETIVOS DEL ESTUDIO:

1) Analizar los resultados obtenidos en términos de morbilidad, mortalidad y supervivencia a largo plazo de una muestra de pacientes ancianos sometidos a cirugía abdominal por cáncer colorrectal.

2) Valorar el papel ejercido por la fragilidad en los resultados a corto plazo (complicaciones y mortalidad operatoria) de una serie de pacientes ancianos de 70 o más años sometidos a distintos procedimientos quirúrgicos abdominales.

3) Valorar el papel ejercido por la fragilidad en los resultados a largo plazo (supervivencia a largo plazo) en una serie de pacientes ancianos de 70 años o más años sometidos a cirugía por cáncer colorrectal.

Para la consecución de estos dos últimos objetivos, se recurrió a la aplicación de las escalas funcionales, instrumentales, cognitivas y nutricionales más comúnmente reportadas, así como comprobar su utilidad en la valoración preoperatoria de los pacientes ancianos de nuestra área asistencial.

RESULTADOS

En esta tesis se expondrán tres estudios consecutivos de carácter descriptivo observacional, llevados a cabo en ancianos de 70 o más años, sometidos a procedimientos gastrointestinales mayores, de forma electiva, en el Servicio de Cirugía General y del Aparato Digestivo del Hospital Universitario de Gran Canaria Doctor Negrín. Si bien los estudios se realizaron de forma secuencial de acuerdo con los objetivos, la publicación de los mismos no refleja dicha secuenciación por los sucesivos cambios que tuvieron que realizarse con vistas a conseguir su aceptación en diferentes publicaciones.

1) Roque-Castellano C, Fariña-Castro R, Nogués-Ramia EM, **Artiles-Armas M**, Marchena-Gómez J. Colorectal cancer surgery in selected nonagenarians is relatively safe and it is associated with a good long-term survival: an observational study. World J Surg Oncol. 2020 Jun 3;18(1):120. doi: 10.1186/s12957-020-01895-8.
2) **Artiles-Armas M**, Roque-Castellano C, Conde-Martel A, Marchena-Gómez J. The Comprehensive Complication Index is Related to Frailty in Elderly Surgical Patients. J Surg Res. 2019 Dec;244:218-224. doi: 10.1016/j.jss.2019.06.011.
3) **Artiles-Armas M,** Roque-Castellano C, Fariña-Castro R, Conde-Martel A, Acosta-Mérida MA, Marchena-Gómez J. Impact of frailty on 5-year survival in patients older than 70 years undergoing colorectal surgery for cancer. World J Surg Oncol. 2021 Apr 10;19(1):106. doi: 10.1186/s12957-021-02221-6.

ARTÍCULO I

Colorectal cancer surgery in selected nonagenarians is relatively safe and it is associated with a good long-term survival: an observational study.

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JCR (2019): Q2 – Factor impacto: 1.96

SJR (2019): Q2 – Factor de impacto: 0.7

World Journal of Surgical Oncology

RESEARCH Open Access

Colorectal cancer surgery in selected nonagenarians is relatively safe and it is associated with a good long-term survival: an observational study

Cristina Roque-Castellano[1], Roberto Fariña-Castro[2], Eva María Nogués-Ramia[1], Manuel Artiles-Armas[1] and Joaquín Marchena-Gómez[1,3*]

Abstract

Background: Advanced age is a risk factor for colorectal cancer, and very elderly patients often need to be surgically treated. This study aimed to analyze the outcomes of a cohort of nonagenarian patients operated on for colorectal cancer.

Methods: Observational study conducted on a cohort of 40 nonagenarian patients, who were treated surgically for colorectal cancer between 2000 and 2018 in our institution. Clinical data, ASA score, Charlson Comorbidity Index, Surgical Mortality Probability Model, tumor characteristics, and nature and technical features of the surgical procedure, were recorded. The Comprehensive Complication Index (CCI) and survival time after the procedure were recorded as outcome variables. Univariate and multivariate analyses were performed in order to define risk factors for postoperative complications and long-term survival.

Results: Out of the 40 patients, 13 (32.5%) were men, 27 (67.5%) women, and mean age 91.6 years (SD ± 1.5). In 24 patients (60%), surgery was elective, and in 16 patients (40%), surgery was emergent. Curative surgery with intestinal resection was performed in 34 patients (85%). In 22 patients (55%), intestinal continuity was restored by performing an anastomosis. The median CCI was 22.6 (IRQ 0.0–42.6). Operative mortality was 10% (4 patients). Cumulative survival at 1, 3, and 5 years was 70%, 47%, and 29%, respectively. In multivariate analysis, only the need for transfusion remained as an independent prognostic factor for complications ($p = 0.021$) and TNM tumor stage as a significant predictor of survival (HR 3.0, CI95% 1.3–7.2).

Conclusions: Colorectal cancer surgery is relatively safe in selected nonagenarian patients and may achieve long-term survival.

Keywords: Colorectal cancer, Nonagenarians, Comprehensive Complication Index, Mortality, Long-term survival

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Introduction

People worldwide are living longer. Today, most people can expect to live into their sixties and beyond and life expectancy is gradually increasing. There is more than a 50% probability that by 2030, the national female life expectancy will break the 90-year barrier, a level that was deemed unattainable by some at the turn of the twenty-first century [1].

Age is a major risk factor for colorectal cancer (CRC), being the third most frequent in the adult population [2]. The incidence of CRC increases with age, with a median age of diagnosis at about 70 years [3]. Specifically, CRC accounts for more than one fifth of the new cases of cancer in people aged 90 years or older. In fact, in women aged 90 or older, the most common sites of cancers are colorectal, breast, and lymphoma/leukemia. In nonagenarian men, CRC is the most frequently observed after prostate cancer [4]. Cancer survival is largely determined by the receipt of a potentially curative treatment, which in the case of CRC is mainly surgery. In these patients, treatment options will depend essentially on the stage of the disease and the health status of patients, which is usually determined by their age, comorbidity, and frailty [5].

It is necessary to highlight that the exclusion of older patients from randomized clinical trials has resulted in a lack of evidence-based guidelines [3]. In the past, nonagenarians with CRC were treated less aggressively because of their age and comorbidity. There was a certain reluctance to submit these patients to a surgical procedure, and some people even considered that no treatment was the best treatment option in this population [6]. Nevertheless, improvements in perioperative management and the development of laparoscopic colorectal surgery have provided great postoperative benefits in the elderly, especially in those older and debilitated. Actually, many of these studies that have shown favorable results regarding morbimortality have reported mainly octogenarian patients [7], being few the series focused on nonagenarian patients.

Only five series have been reported in which nonagenarians with CRC have been exclusively included and most of them with a small number of patients [8–12]. Some other studies have differentiated the characteristics of nonagenarians but in the context of large series that mainly include octogenarians [2, 13, 14].

The aim of this study was to analyze postoperative and long-term outcomes of a cohort of nonagenarians who underwent colorectal cancer surgery in our center, as well as to analyze the factors related to postoperative complications measured by the Comprehensive Complication Index (CCI) and long-term survival.

Methodology

Study design and participants

An observational and longitudinal study was conducted on a cohort of 40 nonagenarian patients who were consecutively treated surgically for CRC between 2000 and 2018 in our institution. The setting was a tertiary care hospital with a catchment population of approximately 400,000 inhabitants. Exclusion criteria included the non-operated nonagenarian patients and those whose clinical records or follow-up was incomplete or not available. The number and characteristics of the non-operated patients were not collected. The data were gathered from the hospital computerized diagnostic coding database and the review of all identified medical records.

Method

A complete clinical history and a preoperative anesthetic assessment were performed on patients who underwent elective surgery. The diagnosis of CRC was carried out by colonoscopy and biopsy. An extension study utilizing thoracoabdominal computed tomography was also performed. The day before surgery, anterograde colon mechanical preparation was implemented as well as preoperative antibiotic prophylaxis 30–60 min before the surgical intervention. Obviously, the patients who required emergency surgery did not meet the requirements mentioned above as colonoscopy, biopsy, and preoperative preparation, except for the antibiotic prophylaxis which was administered in all cases.

The following data were recorded:

Clinical data

The clinical data recorded were age, sex, the American Society of Anesthesiology Physical Status Score (ASA-PS) [15] categorized as ASA-PS I-II vs ASA-PS III-IV, patient comorbidity measured by the Charlson Comorbidity Index [16] and Surgical Mortality Probability Model (S-MPM) [17].

The Charlson Comorbidity Index was calculated preoperatively in each patient using an electronic application [18]. This score includes 19 medical conditions assigned values of 1, 2, 3, or 6, with totals ranging from 0 to 37 points. In general, the absence of comorbidity is considered 0–1 point, low comorbidity 2 points, and high comorbidity ≥ 3 points. In this study, the Charlson Index was not adjusted for age, or for the prevalence of AIDS, as proposed Zavascki and Fusch [19], as there were no cases of this in the study population.

The Surgical Mortality Probability Model (S-MPM) [17] is a simple risk index for all-cause 30-day mortality for noncardiac surgery. The 9-point S-MPM was derived empirically and includes three risk factors: ASA physical status, emergency status, and surgery risk class. Patients with ASA physical statuses I, II, III, IV, or V were assigned either 0, 2, 4, 5, or 6 points, respectively; intermediate or high-risk procedures were assigned 1 or 2 points, respectively; and emergency procedures were

assigned 1. The S-MPM score was categorized as class I (0–4 points), class II (5–6 points), and class III (7–9 points).

Surgical variables

Tumor location (right side vs left side), surgical site where the surgery was performed (colon or rectum), nature of the procedure (elective vs emergency surgery), intent of the surgical procedure (curative vs palliative surgery), performance of anastomosis, and the need for perioperative blood transfusion were the surgical variables. Emergency surgery was defined as surgery within 24 h of admission. Curative surgery was defined as macroscopically complete resection without invasion of the surgical margins at histological examination. Palliative surgery was defined as a surgical procedure designed to alleviate cancer-related symptoms and to prevent the appearance of complications. Based on the need for at least one red blood cell unit transfusion during or immediately before or after the procedure, the patients were classified as transfused or not transfused. The decision to transfuse was based on a liberal transfusion strategy, generally in patients with a hemoglobin concentration ≤ 9 g/dL.

Postoperative complications

Postoperative complications were recorded and graded according to the Comprehensive Complication Index (CCI) [20]. This index is a novel metric of postoperative morbidity, integrating with a single formula, all complications by severity, ranging from 0 (uneventful course) to 100 (death) [21]. The scale represents an improvement on the Clavien-Dindo classification in terms of its association with clinical results. For analysis purposes, the variable was evaluated in two different situations: (a) no complications (CCI = 0) vs. complications (CCI = 1) and (b) as a continuous variable (CCI from 0 to 100).

Operative mortality

It was defined either as any death occurring within 30 days of surgery or any later death that was considered to be a direct consequence of a postoperative complication.

Cancer stage (TNM)

Staging according to the 8th edition of the American Joint Committee on Cancer Staging was collected and categorized from stage I to stage IV.

Long-term survival

It was considered as the period between the performance of the surgical procedure and death or the date of the last follow-up observation before the analysis if the subject was still alive. The mean follow-up of the cohort was 35 months, and the median follow-up was 21 months.

Statistical analysis

Data were analyzed using the statistical package SPSS 17.0 for Windows (SPSS, Chicago, IL, USA). First, a descriptive study of the sample was carried out. Categorical variables were expressed as frequencies and percentages, and the numerical variables by the mean and standard deviation or the median and interquartile range. The survival curves were constructed using the Kaplan-Meier method.

Next, a univariate analysis of both postoperative complications and long-term survival was performed. The sample was also separated into two groups: patients undergoing elective and curative surgery versus patients undergoing urgent and palliative surgery. Both groups were compared. The chi-square test or Fisher's test was used to compare categorical data. For continuous variables, the Mann-Whitney U test, or the Kruskal-Wallis test for nonparametric distributions, was used as appropriate. Linear regression was also used for comparing two continuous variables. Multivariate linear regression was performed on those variables associated with CCI in the univariate analysis to determine their prognostic significance.

In survival analysis, the differences between the survival curves were tested by the log-rank test or by the Tarone-Ware test as appropriate. The relative prognostic significance of the variables in predicting overall survival was assessed using multivariate Cox proportional hazards regression analysis. Hazard ratios were also calculated as association measurements using a Cox regression model. Statistical significance was defined as $p < 0.05$.

Results

Descriptive analysis

Out of the 40 patients in the cohort, 13 (32.5%) were men and 27 (67.5%) were women ($p < 0.001$), with a mean age of 91.6 years (SD ± 1.5 years). Most of the patients lived at home with at least a relative and/or caregiver. Only 3 patients (7.5%) were institutionalized. In 24 patients (60%), surgery was elective, and in 16 patients (40%), surgery was emergent.

Regarding risk scales, only 8 patients (20%) were classified as ASA I-II, and 32 patients (80%) were classified as ASA III-IV. Five patients (13%) were S-MPM grade I, 27 (67%) grade II, and 8 (20%) grade III. According to the Charlson Comorbidity Index, 8 patients (20%) had no comorbidity, 11 (28%) had low comorbidity, and 21 (52%) had high morbidity.

The neoplasm was located in the right colon in 19 cases (47.5%), in the transverse colon in 3 cases (7.5%), in the left colon in 14 cases (35%), and in the rectum in

4 cases (10%). Curative surgery was performed in 34 patients (85%), and palliative surgery was performed in 6 patients (15%), including 4 cases of rectal cancer in whom neoadjuvant chemoradiation therapy was not applied, and 2 patients with liver metastases. In all patients undergoing curative surgery, intestinal resection was performed. In 22 patients (55%), intestinal continuity was restored by performing an anastomosis, while in 18 cases (45%) no anastomosis was carried out. The anastomosis was performed in all patients in whom a right colectomy was performed except in one case, and no anastomosis was performed in all patients operated on for neoplasms in the left side of the colon except in 3 cases. Details of the surgical procedures are shown in Table 1.

In seven cases (17.5%), a laparoscopic approach was carried out to perform the surgical procedure.

Perioperatively, 19 patients (25.2 %) received at least one red blood transfusion. The need for transfusion was not significantly associated with comorbidity measured by the Charlson Index (p = 0.405), but it was associated with the location of the neoplasm (p = 0.001). Patients with malignancies of the right colon required significantly more transfusions than in patients with malignancies of the left colon (69.6% vs 17.6%).

With regard to cancer staging, 28 patients (70%) had non-disseminated disease (stages I–II), 8 patients (20%) were stage III, and 4 patients (10%) were stage IV. All stage IV patients had rectal cancer and underwent palliative surgery.

Only 12 patients (30%) were free of postoperative complications. The remaining 70% had some type of complication, although many of them were minor complications. The mean CCI was 28.7 (± 30.0), and the median CCI was 22.6 (IQR 0.0–42.6). Most patients (57.5%) had a CCI score ≤ 30 (either no complications or minor complications), while 42.5% had serious complications including death. It was remarkable that all patients who reached a CCI score ≥ 60, finally died.

Table 1 Operation types

Operation	*N* (%)
Right colectomy	18 (45%)
Extended right colectomy	1 (2.5%)
Subtotal colectomy	1 (2.5%)
Transversectomy	2 (5.0%)
Sigmoidectomy	3 (7.5%)
Hartmann's procedure	9 (22.5%)
Trans-anal excision	2 (5.0%)
Defunctioning stoma	4 (10.0%)

In 20 patients (50%), *surgical* postoperative complications were registered, with postoperative ileus (19 cases) and wound infection (5 cases) being the most frequently observed. In the 22 patients in whom a primary anastomosis was performed, no suture dehiscence was recorded. Regarding *non-surgical* complications, which occurred in 18 patients (45%), renal failure (16 cases), confusional syndrome (11 cases), and non-fatal infections of different origins (8 cases), were the most frequently observed.

Operative mortality was 10% (4 patients), with three of them being operated on in an emergency setting. In the group of elective surgeries, only 1 patient (4.2%) died. Causes of death were multiorgan failure (2 cases), cardiogenic shock (1 case), and respiratory failure (1 case). Mean stay was 12.5 days (± 6.5 days), and there was no need for reoperation in any patient.

At the end of the follow-up, 11 patients (27.5%) remained alive. Median survival was 26.9 months (IQR 84.4–8.8). Cumulative survival at 1, 3, and 5 years was 70%, 47%, and 29%, respectively (Fig. 1). The survival of the four patients with rectal cancer ranged from 8 months to 2.4 years, and only one of them remained alive at the end of follow-up.

All patients that were discharged returned to the same level of care before the admission at the hospital, but we could not gather information on either their postoperative functional status or their quality of life after the surgical procedure.

Comparative analysis of the two groups

In 21 patients (52.5%), elective and curative surgeries were performed, while in 19 patients (47.5%) emergency and/or palliative surgery were carried out. The differences between both groups are shown in Table 2. Significantly fewer anastomoses were performed in patients in whom palliative or emergency surgery was performed (p < 0.001). The median long-term survival was also significantly lower (p = 0.034) in these patients.

Uni- and multivariate analysis

Univariate analysis of postoperative complications measured by the CCI is shown in Table 3. Age (p = 0.014), palliative surgery (p = 0.002), and need for transfusion (p < 0.001) were associated with CCI—palliative surgery, paradoxically, in a protective sense. By adjusting the three variables in a linear regression model, only transfusion remained as an independent prognostic factor for complications (p = 0.021) (Table 4).

Univariate analysis of long-term survival is shown in Table 5. S-MPM score (p = 0.022, HR 2.4; CI95% 1.1–5.2), emergency surgery (p = 0.022, HR 2.4; CI95% 1.1–5.1), and TNM stage (p = 0.003, HR 3.2; CI95% 1.4–7.2) were associated with a long-term survival. The TNM tumor stage was the only variable that remained as a

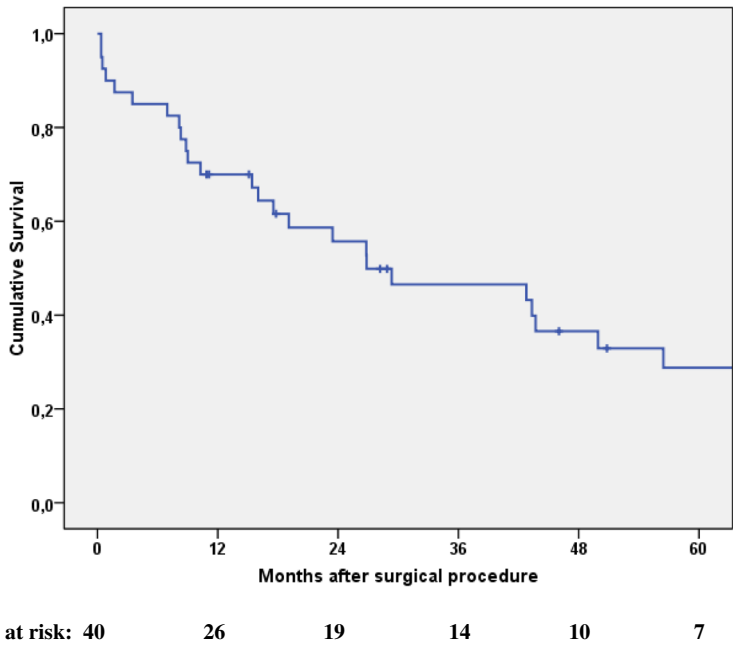

Fig. 1 Overall survival function of the nonagenarian patients operated on by colorectal cancer (Kaplan-Meier)

significant predictor of survival in multivariate analysis (HR 3.0, CI95% 1.3–7.2) (Table 6).

Discussion

The elderly are already the most important group in medical oncology practice. The predictions of aging about this population allow us to foresee that in this age sector, cancer and its treatment will be a first-rate health problem in a few years [1]. The choice of treatment should be based on clinical status, tumor location, comorbidity, and frailty of the patients. In this age sector, this process must be highly individualized since chronological age is not always reflected in biological age.

This study demonstrates that, as is the case with younger patients, a certain number of selected nonagenarian patients with CRC should be considered for curative treatment. Although the postoperative complication rate was high (70%), the median CCI (22.6 points) was not so elevated, and the outcomes obtained in terms of operative mortality and long-term survival were acceptable, especially with elective surgery. Global operative mortality was 10% (4 patients), with the three of them being operated on in an emergency setting. Elective surgery mortality was 4.2%. These results are in accordance with other authors [8, 10, 12, 22], who have reported mortality rates oscillating between 2.1% [8] and 23% [9].

Concerning long-term outcomes, the median overall survival time after colorectal surgery was 26.9 months, which was quite higher than other studies [11] and similar to the 23.92 months reported by Chen et al. [12]. However, the 1-year overall survival rate of 70% reported here is slightly inferior to the 82.6% rate published by Schlichtemeier et al. [10], the series with the best long-term results. In the present study, in line with those published by other authors [8], one third of nonagenarian patients achieved a cumulative survival of 5 years after surgery.

Based on these results, we can support that surgical management of CRC in nonagenarians is associated with acceptable rates of morbidity, mortality, and long-term survival. Therefore, this population should not be denied definitive surgical intervention in both the elective and emergent setting [11], even though emergency surgery is subject to high mortality.

Age has long been considered one of the most important risk factors for postoperative adverse events [3, 8]. The limits of the functional reserve of the organs and tissues in the elderly patient are very narrow and are often exceeded clearly during the perioperative period. In fact, in our series, age was statistically associated with postoperative complications measured by CCI. However, age lost its significance in multivariate analysis and it was not also related to long-term survival. This suggests that other conditions must also be taken into account in predicting worse outcomes in these patients.

Frailty has been proposed as a good predictor of postoperative complications in the elderly patient undergoing a major gastrointestinal procedure [23], but this variable could not be collected due to the retrospective nature of our study. Comorbidity measured by the Charlson Comorbidity Index in the general population has been related to anastomotic leak, postoperative

Table 2 Comparative analysis between the group of patients in whom elective and curative surgery was performed, and the group of patients in whom palliative and/or emergency surgery were carried out

	Total	Elective and curative surgery 21 (52.5%)	Palliative and/or emergency surgery 19 (47.5%)	*p*
Age (mean ± SD)	91.6 (± 1.5)	91.5 (± 1.6)	91.7 (±1.4)	0.737
Gender				0.427
Man	13 (32%)	8 (38.1%)	5 (26.3%)	
Woman	27 (68%)	13 (61.9%)	14 (73.7%)	
Institutionalized	3 (7.5%)	0 (0.0%)	3 (15.8%)	0.098
ASA				0.874
I–II	8 (20%)	4 (19.0%)	4 (21.1%)	
III–IV	32 (80%)	17 (81.0%)	15 (78.9%)	
S-MPM				0.031
I	5 (13%)	3 (14.3%)	2 (10.5%)	
II	27 (67%)	18 (85.7%)	9 (47.4%)	
III	8 (20%)	0 (0.0%)	8 (42.1%)	
Charlson Comorbidity Index				0.065
No	8 (20%)	2 (9.5%)	6 (31.6%)	
Low	11 (28%)	5 (23.8%)	6 (31.6%)	
High	21 (52%)	14 (66.7%)	7 (36.8%)	
Neoplasm location				0.061
Right side[a]	23 (58%)	15 (71.4%)	8 (42.1%)	
Left side	17 (42%)	6 (28.6%)	11 (57.9%)	
Anastomosis				< 0.001
No	18 (45%)	3 (14.3%)	15 /78.9%)	
Yes	22 (55%)	18 (85.7%)	4 (21.1%)	
Transfusion				0.055
No	21 (53%)	8 (38.1%)	13 (68.4%)	
Yes	19 (47%)	13 (61.9%)	6 (31.6%)	
TNM stage				0.112
I–II	28 (70%)	17 (81.0%)	11 (57.9%)	
III–IV	12 (30%)	4 (19.0%)	8 (42.1%)	
CCI (median–IQR)	22.6 (0.0–42.6)	22.6 (10.5–34.1)	12.2 (0.0–54.9)	0.748
Operative mortality	4 (10.0%)	1 (4.8%)	3 (15.8%)	0.246
Median survival in months (IQR)	26.8 (84.4–26.5)	49.9 (99.8–19.1)	17.5 (29.3–8.4)	0.034

[a]Including transverse colon location

complications and death in Chinese patients [24], but there are not published data focused on this topic specifically in nonagenarians. In a previously reported study [25], we found that ASA score and emergency surgery were the most significant factors for operative mortality in a general nonagenarian population, but these variables lost their predictive value for postoperative complications in this subgroup of nonagenarian patients operated on for CRC. Other authors [13] have also reported than older age, higher ASA score, anemia, and lower serum albumin increased postoperative complications. Probably because of the small sample size, these variables and other contributing factors, such as surgical risk according to S-MPM score, and even emergent surgery, were not related to CCI in the present series.

The stage of the disease also did not contribute to raising the morbidity rate, contrary to what was published by other authors [8]. In our series, in those patients who underwent surgery with advanced stages, palliative procedures were only performed. These palliative procedures were accompanied by a few postoperative complications in this very elderly population. However, tumor extension was strongly related to long-term survival.

Table 3 Univariate analysis of risk factors for CCI (Comprehensive Complications Index) 0/1 (no complications vs. complications), and CCI 0–100 score

Risk factors	Total $n = 40$	Complications		CCI 0/1 (p value)	Median CCI (IQR) 22.6 (0.0–42.6)	CCI 0–100 (p value)
		No ($n = 12$) (30%)	Yes ($n = 28$) (70%)			
Age (mean ± SD)	91.6 (± 1.5)	91.1 (± 1.2)	91.8 (± 1.6)	0.110	–	0.014[b]
Gender						
Man	13 (32%)	3 (25.0%)	10 (35.7%)	0.507	22.6 (4.4–77.5)	0.391
Woman	27 (68%)	9 (75.0%)	18 (64.7%)		22.6 (0.0–36.2)	
ASA						
I–II	8 (20%)	3 (25.0%)	5 (17.9%)	0.605	15.7 (0.0–39.2)	0.475
III–IV	32 (80%)	9 (75.0%)	23 (82.1%)		23.4 (0.0–43.7)	
S-MPM						
I	5 (13%)	2 (16.7%)	3 (10.7%)	0.673	22.6 (0.0–61.3)	0.390
II	27 (67%)	8 (66.7%)	19 (67.9%)		22.6 (0.0–32.0)	
III	8 (20%)	2 (16.7%)	6 (21.4%)		45.6 (2.2–89.7)	
Charlson Comorbidity Index						
No	8 (20%)	2 (5.0%)	6 (21.4%)	0.631	33.7 (2.2–56.7)	0.698
Low	11 (28%)	5 (41.7%)	6 (21.4%)		8.7 (0.0–100)	
HIgh	21 (52%)	5 (41.7%)	16 (57.1%)		22.6 (6.1–34.1)	
Neoplasm location						
Right side[a]	23 (58%)	3 (25.0%)	20 (71.4%)	0.006	30.0 (20.9–50.7)	0.015
Left side	17 (42%)	9 (75.0%)	8 (28.6%)		0.0 (0.0–26.7)	
Type of surgery						
elective	24 (60%)	7 (58.3%)	17 (60.7%)	0.919	22.6 (0.0–31.7)	0.576
emergency	16 (40%)	5 (41.7%)	11 (39.3%)		23.4 (0.0–57.8)	
Intent of surgery						0.002
Curative	34 (85%)	7 (58.3%)	27 (96.4%)	0.006	27.5 (8.7–47.3)	
Palliative	6 (15%)	5 (41.7%)	1 (3.6%)		0.0 (0.0–3.1)	
Anastomosis						
No	18 (45%)	8 (66.7%)	10 (35.7%)	0.070	10.5 (0.0–40.9)	0.325
Yes	22 (55%)	4 (33.3%)	18 (64.3%)		23.4 (17.9–45.1)	
Transfusion						
No	21 (53%)	12 (100.0%)	9 (32.1%)	< 0.001	0.0 (0.0–21.8)	< 0.001
Yes	19 (47%)	0 (0.0%)	19 (67.9%)		32.0 (24.2–54.9)	
TNM stage						
I–II	28 (70%)	8 (66.7%)	20 (71.4%)	0.763	22.6 (0.0–36.2)	0.493
III–IV	12 (30%)	4 (33.3%)	8 (28.6%)		26.7 (0.0–88.7)	

[a] Including transverse colon location
[b] Linear regression

Table 4 Multivariate analysis (linear regression) of risk factors associated with Comprehensive Complication Index

	Unstandardized Coefficients		Standardized Coefficients	t	p	95%CI for B
	B	Std. error	Beta			
Constant	− 504.97	253.44	–	− 1.99	0,054	− 1018.9–9.02
Age	5.55	2.77	0.274	2.00	0.053	− 0.07–11.17
Palliative surgery	17.68	11.97	0.213	1.48	0.148	− 6.59–41.95
Transfusion	21.29	8.83	0.359	2.41	0.021	3.38–39.21

B regression coefficient, *t* test statistic, *CI* confidence interval

Table 5 Univariate analysis of long-term survival

	Total (n = 40)	Alives (n = 11) (28%)	Deaths (n = 29) (72%)	p	HR (95%CI)
Age (mean ± SD)	91.6 (± 1.5)	91.5 (± 1.1)	91.7 (± 1.6)	0.310	1.1 (0.9–1.4)
Gender					
Man	13 (32%)	3 (23%)	10 (77%)	0.134	0.6 (0.2–1.2)
Woman	27 (68%)	8 (30%)	19 (70%)		
ASA					
I–II	8 (20%)	4 (50%)	4 (50%)	0.261	1.8 (0.6–5.3)
III–IV	32 (80%)	7 (22%)	25 (78%)		
S-MPM					
I	5 (13%)	2 (40%)	3 (60%)	0.022	2.4 (1.1–5.2)
II	27 (67%)	8 (30%)	19 (70%)		
III	8 (20%)	1 (13%)	7 (87%)		
Charlson Comorbidity Index					
No	8 (20%)	3 (38%)	5 (62%)	0.787	0.9 (0.5–1.4)
Low	11 (28%)	2 (18%)	9 (82%)		
High	21 (52%)	6 (29%)	15 (71%)		
Neoplasm location					
Right side*	23 (58%)	7 (30%)	16 (70%)	0.536	1.3 (0.6–2.7)
Left side	17 (42%)	4 (24%)	13 (76%)		
Type of surgery					
Elective	24 (60%)	8 (33%)	16 (67%)	0.022	2.4 (1.1–5.1)
Emergency	16 (40%)	3 (19%)	13 (81%)		
Intent of surgery					
Curative	34 (85%)	9 (27%)	25 (73%)	0.800	0.9 (0.3–2.6)
Palliative	6 (15%)	2 (33%)	4 (67%)		
Anastomosis					
No	18 (45%)	5 (28%)	13 (72%)	0.099	0.5 (0.2–1.1)
Yes	22 (55%)	6 (27%)	16 (73%)		
Transfussion					
No	21 (53%)	7 (33%)	14 (67%)	0.556	1.3 (0.6–2.6)
Yes	19 (47%)	4 (21%)	15 (79%)		
TNM stage					
I–II	28 (70%)	11 (39%)	17 (61%)	0.003	3.2 (1.4–7.2)
III–IV	12 (30%)	0 (0%)	12 (100%)		

HR hazard ratio
*Including transverse colon location

Table 6 Multivariate analysis (Cox regression) of risk factors associated with a long-term survival

	B	SE	Wald	*p*	HR	95%CI for HR
S-MPM	0.381	0.401	0.906	0.341	1.46	0.67–3.21
Emergency surgery	0.454	0.468	0.939	0.333	1.57	0.63–3.94
TNM stage	0.963	0.436	4.886	0.027	2.62	1.12–6.15

B regression coefficient, *SE* standard error, *Wald* test statistic, *HR* hazard ratio, *CI* confident interval

In this specific group, only the need for blood transfusion was an independent prognostic factor for postoperative complications. This finding could be considered predictable, since the need for blood transfusion would reflect per se the existence of intraoperative complications in many cases. However, in most of our patients, the indication for transfusion was not operative blood loss. Anemia is quite frequently diagnosed in older individuals and constitutes a complex problem. Nutritional deficiency anemias, bleeding anemias, secondary anemias to chronic inflammation status or chronic kidney

disease, clonal anemias, and unexplained anemias, are common in the elderly [26]. Several studies have linked transfusions with many negative outcomes including death in older patients [27, 28]. Ferraris et al. [29] analyzed 8728 non-vascular thoracic operations in patients from 173 hospitals. They found that transfusion of 1 or 2 units of red blood cells increased the risk of composite morbidity, pulmonary complications, systemic sepsis, wound complications, and postoperative length of stay as compared with those who did not receive transfusions. It is not known what is really dangerous, the anemia or the transfusion itself [30], but what is remarkable is that in nonagenarians, these undesirable effects may become even more evident.

There are no previous reports of postoperative morbidity after colorectal surgery using the CCI in these elderly patients. Most of the reported postoperative complications are based on the Clavien-Dindo classification, which considers only the most serious event and underestimates postoperative morbidity as a whole [31]. Previous studies have described relatively high rates of morbidity in the elderly, except Yag et al. [8] which reported 29.2%, which was quite lower than our 70%. This may be related to the proportion of elective patients included in this last series, which was much higher than other studies (79.2%) and may reflect the low perioperative mortality and morbidity rates. Our cohort had more emergent surgeries, and it is remarkable that all kinds of complications, even minor adverse events, were collected. It is well known that the postoperative complication rate is higher in elderly patients who underwent emergent open surgeries, ranging from 27.6 to 81% [12]. Therefore, it would be advisable to avoid emergency surgery as much as possible and to offer therapeutic alternatives, such as the placement of colonic stents. This would improve the clinical and nutritional status of patients prior to elective surgery, which should benefit these patients [2].

The most frequent complication in the present study was postoperative ileus, which is quite frequent in this age group. In other series, postoperative confusion prevails [22], which is often difficult to assess and whose actual frequency of presentation can be masked in the surgical setting. Respiratory complications, renal failure, and surgical site infection have also been reported as frequent complications in nonagenarians [11].

In the present study, the procedure most frequently performed was right colectomy followed by the Hartmann procedure, which was in line with other series [8, 11, 22]. Available studies suggest that tumors are more likely to be right-sided in nonagenarian patients [2, 10]. Right colectomy seems to be less aggressive and better tolerated by very elderly people. However, we had more complications in patients operated on for right-sided lesions than in patients with left-sided lesions. Despite the fact that no anastomotic leak was observed, it should be noted that many of these patients with right side lesions were preoperatively anemic and hypoproteinemic. They required significantly more transfusions, which probably made them more susceptible to all kinds of postoperative complications.

There was also better survival in patients with right-sided tumors, but it did not reach statistical significance. Regarding the lesions in a low rectal location, no patient underwent radical surgery in our series. Also, they were not given neoadjuvant or adjuvant chemoradiation. Only local conservative treatment was applied, obtaining acceptable results in terms of long-term survival for the age.

In a large cohort of older patients operated on in California and reported by Kunitake et al. [2], an abdominoperineal resection was performed only in 16.4% of nonagenarians. In another series with less patients [8], 2 of 48 nonagenarians were submitted to this procedure. It is worth noting that Kunitake et al. [2] reported a 0.7% rate of sigmoidectomies vs. a 45.5% rate of rectal anterior resection procedures in the subgroup of nonagenarians. This circumstance suggests that the term “anterior resection of the rectum” could be preferably used in nonagenarian patients with cancer of the rectosigmoid junction or even sigmoid colon.

Anastomosis should be considered a safe surgical procedure in nonagenarian patients, at least in right colectomies. Despite having performed 18 anastomoses on the right colon and 3 on the left colon, no leaks were found. These results are consistent with those published by other authors in the few series reported that address detailed information on colorectal surgery in nonagenarians [11, 22]. Only one anastomosis leak after a right colectomy was recorded by Yap et al. [8], without mortality. Thus, surprisingly, the rate of anastomosis leakage is very low or nonexistent. These results are indicating that we should not contraindicate an anastomosis only considering age as a possible factor related to anastomotic leakage.

Laparoscopic surgery is considered an extremely useful treatment for very old patients because it has a low risk of postoperative complications, even in the presence of pre-existing diseases [14].

Yap et al. [8] reported a laparoscopic-assisted operation in 41.7% of their patients with good outcomes. They found that patients undergoing open surgery were more likely to have perioperative complications than patients undergoing minimally invasive surgery, and the mortality rate was 0%. In the present study, only 17% of patients were operated on using a laparoscopic approach, with no deaths, although this percentage has been increasing in recent years. This confirms that, even in patients > 90 years old, laparoscopic surgery for colorectal cancer is

safe. Moreover, laparoscopy seems to improve postoperative outcomes in the elderly as compared with younger patients [32].

On the other hand, there are few studies that evaluate the outcomes in terms of toxicity and survival among nonagenarian patients with CRC treated with chemotherapy or concurrent chemoradiation therapy. Reddy et al. [33] reported that despite the high rate of treatment toxicity, selected octogenarian and nonagenarian patients could benefit from chemotherapy. However, in this study, which does not distinguish between octogenarians and nonagenarians, the exact role that chemotherapy could play in nonagenarian patients is not clear. In other studies [22], no patients in this age group received adjuvant therapy.

Compared with other age groups, it is evident that most surgeons are considerably less aggressive with these older patients in the presence of metastatic disease [10]. Nevertheless, it has been an important advance to not systematically deny colorectal cancer surgery in nonagenarian people.

Elective surgery, SMPM score, and the extent of the colorectal neoplasia were related to the long-term survival in the present series. However, only TNM stage was determined to be an independent prognostic factor for survival. The tumor stage being the most determining factor in long-term survival, in line with other studies [12], demonstrates that this population will behave oncologically in a similar way to younger groups of patients with CRC.

In order to identify other factors that delimited the type of elderly patient who would most benefit from surgery in colorectal cancer, the patients were also separated into two groups according to the surgical procedure performed: curative and elective surgery vs palliative and/or emergency surgery. However, neither biodemographic factors nor any preoperative clinical variable could help demonstrate possible differences between these two groups, probably because of the limited number of patients.

The limitations of the study include its retrospective nature, the relatively small size of the series, the unknown proportion of patients with colorectal cancer who were not operated on and were referred for palliative care, and the lack of postoperative quality of life assessment. On the other hand, preoperative geriatric assessment has become a powerful tool that could help to understand what type of patients would benefit the most from the surgical treatment. Due to the retrospective nature of the study design, these data were not evaluated. The strengths of this study include the availability of detailed perioperative information on the oldest population treated in our department, the long follow-up of this cohort, and the hopeful long-term outcomes, which can be extrapolated to the general population of nonagenarians.

Conclusion

We support that advanced age, per se, is not a disease and should never be a contraindication for a surgical procedure in patients with CRC. Moreover, we consider that chronological age serves as a poor substitute for biological age, which in itself is difficult to define or determine. We conclude that colorectal cancer surgery is relatively safe in selected nonagenarian patients and may achieve a long-term survival.

Acknowledgements
Not applicable

Authors' contributions
CRC: contributed to writing the manuscript. RFC: data collection, contributed to writing the manuscript. ENR: data collection. MAA: data analysis, contributed to writing the manuscript. JMG: design, statistic analysis, and coordination. The authors read, commented, and approved the manuscript.

Funding
Not applicable

Availability of data and materials
Not applicable

Ethics approval and consent to participate
The study was approved by the Hospital Ethics Committee (Code 120273).

Consent for publication
Not applicable

Competing interests
The authors declare that they have no competing interests.

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Received: 1 April 2020 Accepted: 25 May 2020
Published online: 03 June 2020

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Publisher's Note

ARTÍCULO II

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Artiles-Armas M, Roque-Castellano C, Conde-Martel A, Marchena-Gómez J. The Comprehensive Complication Index is Related to Frailty in Elderly Surgical Patients. J Surg Res. 2019 Dec;244:218-224.

JCR (2019): Q3 – Factor de impacto: 1.841

SJR (2019): Q1 – Factor de impacto: 0.79

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.JournalofSurgicalResearch.com

Research review

The Comprehensive Complication Index is Related to Frailty in Elderly Surgical Patients

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ARTICLE INFO

Article history:
Received 18 February 2019
Received in revised form
3 May 2019
Accepted 5 June 2019
Available online xxx

Keywords:
Comprehensive complication index
Elderly
Frailty
Post-operative outcome

ABSTRACT

Background: Frailty has been proposed as an independent risk factor for predicting post-surgical outcomes in elderly surgical patients. The Comprehensive Complication Index (CCI) seems to be the most widely used grading of individual complications in many surgical fields. The objective of this study was to evaluate the association of frailty, measured by Canadian Study of Health and Aging–Clinical Frailty Scale (CSHA-CFS), with the CCI in the elderly surgical patient.

Material and methods: A prospective cross-sectional study was carried out in 256 patients aged ≥70 y who underwent major gastrointestinal surgery. Sociodemographic characteristics, baseline disease, CSHA-CFS, and medical/surgical complication using the Comprehensive Comorbidity Index were evaluated. We hypothesized that frailty measured by CSHA-CFS and the CCI are associated.

Results: Of 256 patients, 154 (60%) were men and 102 (40%) were women, with mean age of 76.1 y (SD ± 5.1). One-hundred and eighty-five patients (74%) underwent surgery for a malignant cause, and 97 patients (38%) had some degree of frailty. Mean CCI was 16.1 (SD ± 23.0). Postoperative mortality was 3%. Pondering the scale CCI 0-100, frailty correlated well with postoperative complications ($P = 0.035$). For patients who developed at least 1 complication, for each unit that the CSHA-CFS was raised, the CCI increased by 5.2 points ($P = 0.002$). The multivariate analysis showed that the CSHA-CFS was the only independent prognostic factor associated with postoperative CCI in this series.

Conclusions: Frailty determined by CSHA-CFS is closely associated with the CCI, being a good predictor of postoperative complications in the elderly patient operated on by a major gastrointestinal procedure.

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https://doi.org/10.1016/j.jss.2019.06.011

Introduction

Estimates suggest that about 16% of the world's population will be aged over 65 y by the year 2050,[1] so the demand for health care is expected to increase significantly in the coming decades. More than 75% of people over 65 y have at least one chronic disease. Many of these pathologies (cancer, joint degeneration, coronary artery disease, etc.) benefit from surgical treatment, yet as more and more elderly patients undergo an intervention, it is producing a clear increase in all-cause complications and mortality.[2]

Frailty has recently been demonstrated as an independent risk factor for predicting postsurgical outcomes in elderly patients undergoing vascular, cardiac, and gastrointestinal major interventions.[3-6] A meta-analysis of more than one million patients undergoing major abdominal surgery has showed the relation of frailty with increased postoperative mortality and morbidity.[7] The concept of frailty has been defined as a multifactorial syndrome characterized by a decreased reserve and resistance to stressors resulting from cumulative decline in multiple physiological systems and causing vulnerability to adverse outcomes.[8] However, even if the literature includes several scales used to define frailty in surgical patients, there is no single gold standard measure of frailty.[9-11]

In 2005, the Canadian Study of Health and Aging—Clinical Frailty Scale (CSHA-CFS)[12] was developed as a new tool to predict death or need for institutional care. This scale was applied to elderly patients who participated in the second stage of the CSHA, and it is now recognized as a reliable instrument in the detection of frailty in a medical setting. The CSHA-CFS is simple to administer and correlates well with the more thorough frailty index which has been shown to predict morbidity and mortality in some surgical populations.[13] However, few studies have focused on the application of the CSHA-CFS in surgical patients, despite being a simple, less time-consuming and reliable test.[12,14]

On the other hand, Comprehensive Complication Index (CCI) summarizes the results classified by the Clavien-Dindo classification (CDC) on a numerical scale weighted by severity.[15] The scale represented an improvement on the CDC in terms of its association with clinical results. The CCI has been recently validated in all the surgical interventions performed at a General Surgery department,[16,17] as well as economically.[18]

The association of frailty with CCI in the aging population has been not previously reported in the literature. We hypothesized that frailty measured by CSHA-CFS and the CCI are associated. The aim of this study was to evaluate the possible relationship between both indices, CSHA-CFS and CCI.

Materials and methods

A prospective, cross-sectional, observational study was conducted on 256 consecutives over 70-y-old patients who underwent abdominal surgery between January 2013 and August 2016. The setting was a tertiary-care hospital that attends a population of approximately 400,000 people. Patients who were operated on either under emergency conditions, or in the outpatient surgery, were excluded. The study was approved by the Ethics Committee of the Hospital (Code 140195).

A surgeon and an anesthesiologist preoperatively evaluated all patients. All patients consented to participate in the study.

A history, physical examination, and a comprehensive geriatric assessment were carried out to discover possible signs of frailty based on CSHA-CFS.[12]

Laboratory tests, chest X-rays, electrocardiograms, and additional tests were also performed according to each patient's underlying condition. The anesthesiologist did not normally contraindicate anesthesia if the surgeon and family had agreed to undergo the procedure despite the presence of comorbidity or frailty.

Data were collected prospectively and recorded in a database. The following predictive variables were evaluated.

Patient characteristics: age, gender

Regarding the age cutoff point, although CSHA-CFS was initially developed for a population ≥65 y old,[12] the progressive increase in life expectancy has lead us to consider it appropriate to include patients aged ≥70 y, 5 y older than the World Health Organization definition for the elderly population.

Charlson comorbidity index

It was calculated preoperatively for each patient using an electronic application.[19] This score includes 19 medical conditions assigned values of 1, 2, 3, or 6, with totals ranging from 0 to 37 points. In general, the absence of comorbidity is considered: 0-1 points; low comorbidity: 2 points; and high comorbidity: ≥3 points.[20] In this study, the Charlson comorbidity index has not been adjusted for age,[20] or for the prevalence of AIDS,[21] as there are no cases of this in the study population.

Baseline disease (benign versus malignant)

The presence of a malignant neoplasm was recorded if it was the main indication for the surgical procedure.

CSHA—Clinical Frailty Scale (CSHA-CFS)

This frailty scale proposed by Rockwood *et al.*[12] were based on a 1 to 7 numerical scale as follows: CFS 1 (very fit), CFS 2 (well), CFS 3 (well with treated comorbid disease), CFS 4 (apparently vulnerable), CFS 5 (mildly frail), CFS 6 (moderately frail), and CFS 7 (severely frail). This information was obtained within 24 h of admission and before surgery. In this study, the threshold for determining frailty was a CSHA-CFS ≥4. It has been recently suggested that this cutoff of four was the most strictly correlated with postoperative outcome.[22]

Comprehensive Complication Index (CCI)

This index, described in 2013, incorporates all complications and their severity as recorded by the CDC, and summarizes the

postoperative course on a continuous scale (0-100).[15] The CCI was considered the outcome variable. This determination was obtained 30 d after the procedure. This variable was evaluated in three different situations: a) No complications (CCI = 0) *versus* complications (CCI = 1); b) As a continuous variable: CCI from 0 to 100 scale; and c) only patients in which CCI ≥ 1.

Both, CSHA-CFS and CCI, were recorded by a single surgeon. Neither the patients nor their primary care doctors were notified about the degree of frailty.

Statistical analysis

The data were analyzed using the statistical package SPSS 17.0 for Windows (SPSS, Chicago, IL). First, the sample was descriptively analyzed. The categorical variables were summarized as frequencies and percentages; continuous variables were described as means and standard deviations (SDs) when the data followed a normal distribution, or medians and interquartile ranges (IQR) when they did not. The Kolmogorov–Smirnov test was applied to evaluate the distribution of values in continuous variables.

Univariate analysis was performed to identify the predictive variables associated with postoperative complications (CCI). The chi-squared test or Fisher's test were used to compare categorical data. For continuous variables, the Mann–Whitney *U* test, or the Kruskal–Wallis test for nonparametric distributions, were used as appropriate. Linear regression was also used for comparing two continuous variables.

Multivariate analysis by stepwise linear regression was then performed on those variables associated with CCI by univariate analysis to determine their prognostic significance.

A *P*-value <0.05 was considered statistically significant. Odds ratio and a 95% confidence interval (95% CI) were also calculated for significant variable associations where appropriate.

Results

Of 256 patients, 154 (60%) were men and 102 (40%) were women. Patients had a mean age of 76.1 y (SD ± 5.1).

Type of surgery performed

The following operations were performed: 171 cases (66.8%) of colorectal surgery, 44 cases (17.2%) of biliary surgery, 17 cases (6.6%) of esophagogastric surgery, 5 cases (2.0%) of hepatic surgery, 10 cases (3.9%) of pancreatic surgery, 3 splenectomies (1.2%), 2 adrenalectomies (0.8%), and a group of 4 (1.6%) miscellaneous procedures. To facilitate the statistical analysis, this variable was categorized into colorectal surgery, hepato-pancreatic-biliary surgery, esophagogastric surgery, and other types of procedures.

Baseline disease

In total, 189 (74%) were operated on for neoplasms and 67 (26%) for non-neoplastic pathologies.

Comorbidity

The median score for the Charlson comorbidity index was 3.0 (IQR 2.0-4.0). Forty-one patients (16%) did not present comorbidity (0-1 points), 85 patients (33%) had low comorbidity (2 points), and 130 patients (51%) had high comorbidity (≥3 points).

Frailty (CSHA-CFS)

The median CSHA-CFS score was 3.0 (IQR 3.0-5.0). A total of 159 patients (62%) were considered as having no frailty, and 97 patients (38%) had some degree of frailty.

Comprehensive Complications Index

Including minor complications, at least 1 complication (CCI = 1) occurred in 125 patients (49%), whereas in 131 patients (51%), there were no postoperative complications (CCI = 0). Mean CCI (from 1 to 100 scale) was 16.1 (SD ± 23.0) and median CCI was 0.0 (IQR: 0.0-22.6) (Figure). When considering only complicated patients (CCI ≥ 1), mean CCI was 32.9 (SD ± 23.0) and median CCI was 22.6 (IQR: 20.9-45.7). In this series, 28.5% of patients developed some medical complication, mainly postoperative ileus (22 patients), renal failure (10 patients), or pneumonia (7 patients). On the other hand, 26.6% developed some surgical complication, being the most frequent: postoperative bleeding (17 patients), anastomotic dehiscence (15 patients), and wound infection (11 patients).

Operative mortality

Seven patients (3%) died within 30 d of surgery. The following procedures were performed on these patients: right hemicolectomy due to cancer (3 patients), left hemicolectomy due to cancer (1 patient), anterior resection for rectal cancer (1 patient), small bowel resection with eventroplasty (1 patient), and finally, thoracoscopy and laparoscopy exploratory for esophageal cancer with incidental peritoneal carcinomatosis (1 patient). The causes of death were anastomotic dehiscence

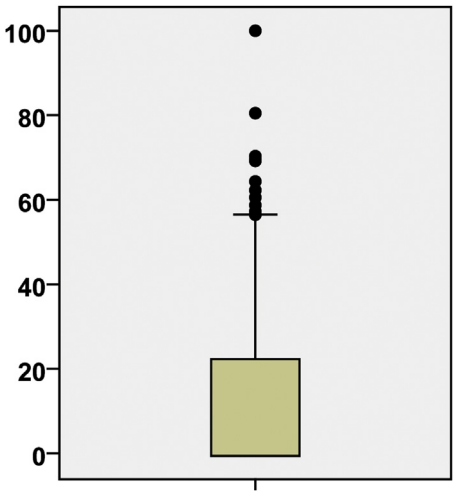

Figure – Boxplot distribution of CCI 0-100. (Color version of figure is available online.)

Table 1 – Univariate analysis of risk factors for CCI 0/1 (no complications *versus* complications), CCI 0-100, and CCI ≥ 1.

Risk factors	Total	Complications		CCI 0/1 (*P*-value)	CCI 0-100 (*P*-value)	CCI ≥1 (*P*-value)
		No ($n = 131$)	Yes ($n = 125$)			
Age (mean ± SD)	76.1 ± 5.0	76.6 ± 5.1	75.6 ± 4.8	0.141	0.459	0.564
Gender				0.001	<0.001	0.186
Man	154 (60%)	66 (50.4%)	88 (70.4)			
Woman	102 (40%)	65 (49.6%)	37 (29.6%)			
Type of surgery				0.005	0.007	0.807
Colorectal	171 (66.8%)	78 (59.5%)	93 (74.4%)			
HPB	59 (23.0%)	42 (32.1%)	17 (6.6%)			
Esophagogastric	17 (6.6%)	8 (6.1%)	9 (7.2%)			
Other	9 (3.5%)	3 (1.2%)	6 (4.8%)			
Neoplasia				0.013	0.044	0.378
No	67 (26.2%)	43 (32.8%)	24 (19.2%)			
Yes	189 (73.8%)	88 (67.2%)	101 (80.8%)			
Charlson comorbidity index				0.001	0.002	0.857
No	41 (16.0%)	31 (23.7%)	10 (8.0%)			
Low	85 (33.2%)	45 (34.4%)	40 (32.0%)			
High	130 (50.8%)	55 (42.0%)	75 (60.0%)			
Frailty (CSHA-CFS) (Median-IQR)	3.0 (3.0-5.0)	3.0 (3.0-5.0)	3.0 (3.0-5.0)	0.999	0.035	0.002

HPB = hepato-pancreatic-biliary.

(2 patients), catheter-related bloodstream infection (1 patient), pneumonia (1 patient), cardiogenic shock (1 patient), venous mesenteric ischemia due to massive venous thrombosis (1 patient), and 1 patient with progression of unresectable peritoneal metastasis.

Univariate analysis

Table 1 shows the results of the univariate analysis in the three situations in which the CCI was considered. Frailty (CSHA-CFS) was not a good predictor of complications comparing CCI = 0 *versus* CCI = 1 ($P = 0.99$). However, both when considering the CCI scale from 0 to 100 (CCI, 0-100) ($P = 0.035$), and when considering only patients who developed at least one complication (CCI ≥ 1) ($P = 0.002$), we found a statistically significant association between frailty and the appearance of postoperative complications.

Pondering the scale CCI 0-100, CSHA-CFS correlated well with postoperative complications ($R^2 = 0.017$, B coefficient: 2.5—95% CI: 0.2-4.9; $P = 0.035$). Nevertheless, among patients who developed at least 1 complication (CCI ≥ 1), CSHA-CFS predicted much better the number and severity of complications: for each unit that CSHA-CFS was raised, CCI increased by 5.2 points ($R^2 = 0.072$, B coefficient: 5.2—95% CI: 1.8-8.5, $P = 0.002$).

Age correlated with CSHA-CFS ($P = 0.001$).

Considering operative mortality, patients who died had a mean CSHA-CFS of 5.14 (SD ± 1.07) and a median CSHA-CFS of 5 (IQR: 5-6) compared with patients who survived, whose mean CSHA-CFS was 3.91 (SD ± 1.19) and a median CSHA-CFS of 3 (IQR: 3-5). These differences were statistically significant ($P = 0.007$). A complementary univariate and multivariate analysis were not performed with mortality as output variable due to lack of statistical power because only 7 of 256 patients died.

Table 2 – Linear regression.

Risk factors	B	SE	Beta	t	P	95% CI for B
(Constant)	15.740	10.416	-	1.511	0.133	−4.9 to 36.4
Frailty (CSHA-CFS)	5.167	1.686	0.269	3.065	0.003	1.8 to 8.5
Gender	−6.785	4.387	−0.135	−1.547	0.125	−15.5 to 1.9
Neoplasia	−0.223	5.419	−0.004	−0.041	0.967	−10.9 to 10.5
Charlson comorbidity index	−0.410	3.335	−0.011	−0.123	0.902	−7.0 to 6.2

Dependent variable: CCI ≥ 1.
B = regression coefficient; SE = standard error; t = statistic test.

Multivariate analysis

Table 2 shows that frailty (CSHA-CFS) was the only independent prognostic factor associated with postoperative CCI in this series when considering only patients who developed at least one complication (CCI $\geq$ 1) ($P = 0.003$; 95% CI for B coefficient: 1.8-8.5). Neither the gender ($P = 0.125$), the existence of neoplasia ($P = 0.967$) nor the Charlson comorbidity index ($P = 0.902$) were independent predictors for the development of postoperative complications.

Discussion

As the population ages, the rate of performing surgical procedures in the elderly population also increases. More than 50% of surgical procedures are performed for individuals aged >65 y.[23] Currently, there are no clear criteria to define whether an elderly patient can overcome a major gastrointestinal intervention. According to current evidence, preoperative frailty may be associated with postoperative morbidity in geriatric patients and is a better predictor than age alone in many surgical populations.[7]

Therefore, assessing frailty in elderly surgical patients is considered essential to provide a realistic estimation of their short- and long-term outcomes depending on the planned intervention. A recent meta-analysis revealed that preoperative frailty implies a 2.77 times greater risk of 30-day mortality and 1.99 times greater risk of 1-year mortality after surgical interventions.[24] These results are supported by those of two other recently published systematic review and meta-analysis with a similar objective; that is, frailty was associated with increased mortality, postoperative complications, prolonged length of stay, and discharge to residential care facilities.[11,25] Nevertheless, although the American College of Surgery recommends the assessment of frailty in the preoperative setting, the definition and measurement criteria for preoperative frailty remain unclear.[26,27]

Rockwood *et al.*[12] claimed that CSHA-CFS was an effective measure of frailty, which provides predictive information about death in the elderly population and is similar to other established tools. Although this study did not aim to compare CSHA-CFS with other scales of frailty, CSHA-CFS has certain advantages such as being less time consuming, validated, and easy to perform.[14] Comparatively, Eamer *et al.*[28] reported this scale was less cumbersome than the frailty phenotype, also demonstrating very good inter-rater reliability.[29] In turn, Ritt *et al.*[30] communicated that the CSHA-CFS was the best predictor for 1-year mortality in a nonsurgical elderly population after being compared with the rest of the frailty scores studied. However, perhaps the main disadvantage attributed to CSHA-CFS is that it does not clearly define each category.

There are less data on the preoperative use of this risk scale in a population composed of only elderly patients undergoing nonurgent digestive surgery.[22] Currently, the results derived from the preoperative use of this risk scale in a population composed solely of elderly patients undergoing nonurgent digestive surgery remain unknown. However, it has been recently suggested that in the future, a more targeted strategy to improve postoperative outcomes may be facilitated using CSHA-CFS.[14] Based on our results, we confirm the high predictive ability of CSHA-CFS in terms of postoperative morbidity in elderly patients who undergo elective major gastrointestinal surgery.

Age is widely used as a predictor of mortality in several multivariable studies, although with disparate results.[13] It is easy to consider that an increase in mortality reflects, to some extent, an increase in frailty associated with senescence. Therefore, the association between postoperative short-outcomes and age of a patient when compared with others within the same age group, could vary because of that person's frailty, implying that not all patients of the same age have the same risk of having a complication.[31] López-Soto and Formiga[32] reported that between 10% and 20% of people aged >65 y were frail, whereas these values increased to >50% in octogenarians and were even higher in nonagenarians. Therefore, frailty is clearly associated with age. However, based on our results and those of other authors, we believe that frailty rather than age alone is actually a more reliable predictor of surgical risk.

On the other hand, while CDC is focused only on the most severe complication, CCI incorporates all complications and their severity as recorded CDC, summarizing the postoperative course on a numerical scale.[15] Thus, a limitation of CDC is that less-severe events may not be considered, leading to an underestimation of the true overall postoperative morbidity.[16] Both CDC and CCI appear to be correlated with all parameters; however, CCI shows a significantly higher correlation with hospital stay and reintervention than CDC.[17]

Until now, the possible association between frailty and CCI in elderly has not been assessed. Van der Windt *et al.*[33] reported data of a prospective study performed in 162 patients who underwent hepatopancreatobiliary surgery that aimed to validate the Risk Analysis Index (RAI) for frailty in predicting morbidity determined by CCI. They also found an association between both scores, although the population examined did not include elderly individuals. RAI did not directly predict if postoperative morbidity would occur or not (comparing CCI = 0 *versus* CCI $\geq$ 1), and the CCI score was correlated with RAI only if patients without postoperative complications were not included in the analysis.

CCI is usually analyzed by different methods by different authors.[16,17,33,34] In our analysis, we assessed the association between frailty (CSHA-CFS) and CCI in three possible scenarios: CCI = 0 *versus* CCI $\geq$ 1; CCI 0-100; and only CCI $\geq$ 1.

Based on our results, frailty (CSHA-CFS) was not a good predictor of complications when comparing CCI = 0 *versus* CCI $\geq$ 1. Nevertheless, regarding the CCI 0-100 scale, CSHA-CFS correlated well with postoperative complications. Moreover, among patients who developed at least 1 complication (CCI $\geq$ 1), CSHA-CFS predicted much better the number and severity of complications. For each unit that CSHA-CFS increased, CCI increased by 5.2 points, which was better than that proposed previously for the RAI score.[33] In addition, frailty determined by CSHA-CFS was the only independent prognostic factor associated with postoperative CCI in elderly patients who underwent a major gastrointestinal procedure via an elective way and thus is a better predictor of complications than other

indices such as the Charlson comorbidity index, existence of neoplasia, or type of surgery.

These results indicate that frailty does not directly predict whether a complication will occur or not, but once it occurs, it can predict with high accuracy the incidence of additional and more serious complications.

Frailty must not be considered an absolute contraindication for surgery. Detecting frail patients with a high risk for developing postoperative complications provides the opportunity to preoperatively optimize their physiological status through prehabilitation interventions,[33] as well as foresee the implementation of appropriate rehabilitation measures in the postoperative period. Moreover, early detection of this type of patients could result in a torpid postoperative period, thus allowing us to inform appropriately the potential risk of complications, manage health care resources, and reduce health care costs derived from their care.[34]

The operative mortality in our series was low (3%), which was similar to previously reported data.[24,35] The rate of postoperative complications according to CCI was greater than that globally reported (49%), which ranges between 24% and 38.6% in the general population.[3,16,17,31,33] However, if we focus on studies conducted in very elderly patients, we observe that this rate of postoperative complications reaches 49.2%-60%.[36,37]

This is a monocentric study, and a larger sample size would probably reveal more independent predictor variables of postoperative short-outcomes. Conversely, although Eamer *et al.*[29] showed a good inter-rater reliability in determining frailty using CSHA-CFS, biases derived from data collection by a single surgeon cannot be ruled out. Some patient or intraoperative characteristics, such as new-onset weight loss, history of recent falls, or length of surgery, have not been included in this study; thus, these factors could be confounders. In turn, a selection bias could be incurred by the surgeon at the time of offering the surgery to this patient group. Finally, in this study, neither the patients nor their primary care doctors were notified about the degree of frailty, although the need for clinicians in primary care to identify frail patients using CSHA-CFS has been recently suggested.[14] Despite these limitations, we could demonstrate the predictive power of frailty (CSHA-CFS) in terms of postoperative morbidity determined by CCI. In addition, this prospective study included consecutive patients who all agreed to participate. Therefore, we believe that our results could be generalized to other surgical patient populations.

Conclusions

This is the first study to demonstrate an association between frailty using CSHA-CFS and CCI. Frailty is closely associated with CCI and is a good predictor of postoperative complications in the elderly patients who undergo major gastrointestinal procedures. Despite its apparent limitations, CSHA-CFS is an underappreciated, easy, and feasible prognostic indicator. By considering each complication that occurred and not just the ones of greater degree, the correlation demonstrated with CCI provides individualized information of each elderly patient and facilitates the decision-making for these types of procedures.

Acknowledgment

Authors' contributions: M.A-A. and J.M-G. contributed to conceptualization, methodology, software, validation, formal analysis, investigation, resources, data curation, writing—original draft, writing—review and editing, visualization, and project administration. C.R-C. and A.C-M. contributed to conceptualization, methodology, validation, supervision, and writing—review and editing.

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Disclosure

The authors report no proprietary or commercial interests in any product mentioned or concept discussed in this article.

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ARTÍCULO III

Impact of frailty on 5-year survival in patients older than 70 years undergoing colorectal surgery for cancer.

Artiles-Armas M, Roque-Castellano C, Fariña-Castro R, Conde-Martel A, Acosta-Mérida MA, Marchena-Gómez J. Impact of frailty on 5-year survival in patients older than 70 years undergoing colorectal surgery for cancer. World J Surg Oncol. 2021 Apr 10;19(1):106.

JCR (2019): Q2 – Factor impacto: 1.96

SJR (2019): Q2 – Factor de impacto: 0.7

Artiles-Armas et al. World Journal of Surgical Oncology (2021) 19:106
https://doi.org/10.1186/s12957-021-02221-6

World Journal of Surgical Oncology

RESEARCH Open Access

Impact of frailty on 5-year survival in patients older than 70 years undergoing colorectal surgery for cancer

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Abstract

Background: Frailty has been shown to be a good predictor of post-operative complications and death in patients undergoing gastrointestinal surgery. The aim of this study was to analyze the differences between frail and non-frail patients undergoing colorectal cancer surgery, as well as the impact of frailty on long-term survival in these patients.

Methods: A cohort of 149 patients aged 70 years and older who underwent elective surgery for colorectal cancer was followed-up for at least 5 years. The sample was divided into two groups: frail and non-frail patients. The Canadian Study of Health and Aging-Clinical Frailty Scale (CSHA-CFS) was used to detect frailty. The two groups were compared with regard to demographic data, comorbidities, functional and cognitive statuses, surgical risk, surgical variables, tumor extent, and post-operative outcomes, which were mortality at 30 days, 90 days, and 1 year after the procedure. Univariate and multivariate analyses were also performed to determine which of the predictive variables were related to 5-year survival.

Results: Out of the 149 patients, 96 (64.4%) were men and 53 (35.6%) were women, with a median age of 75 years (IQR 72–80). According to the CSHA-CFS scale, 59 (39.6%) patients were frail, and 90 (60.4%) patients were not frail. Frail patients were significantly older and had more impaired cognitive status, worse functional status, more comorbidities, more operative mortality, and more serious complications than non-frail patients. Comorbidities, as measured by the Charlson Comorbidity Index ($p = 0.001$); the Lawton-Brody Index ($p = 0.011$); failure to perform an anastomosis ($p = 0.024$); nodal involvement ($p = 0.005$); distant metastases ($p < 0.001$); high TNM stage ($p = 0.004$); and anastomosis dehiscence ($p = 0.013$) were significant univariate predictors of a poor prognosis on univariate analysis. Multivariate analysis of long-term survival, with adjustment for age, frailty, comorbidities and TNM stage, showed that comorbidities ($p = 0.002$; HR 1.30; 95% CI 1.10–1.54) and TNM stage ($p = 0.014$; HR 2.06; 95% CI 1.16–3.67) were the only independent risk factors for survival at 5 years.

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Conclusions: Frailty is associated with poor short-term post-operative outcomes, but it does not seem to affect long-term survival in older patients with colorectal cancer. Instead, comorbidities and tumor stage are good predictors of long-term survival.

Keywords: Frailty, Geriatrics, Colorectal cancer, Comorbidity

Introduction

An ageing population is increasing the demand for healthcare. More than 4 million major surgical operations are performed annually in the USA on older patients, yet as an increasing number of geriatric patients undergo surgery, there is a clear increase in age-related peri-operative morbidity and mortality [1]. Many of these operations are surgical procedures to treat older patients with colorectal cancer (CRC). In fact, colorectal cancer is the third most common cancer in the world, and surgery, with either curative or palliative intent, is the main treatment modality for this disease. Approximately 60% of CRC patients are > 70 years old at the time of diagnosis, and 43% are > 75 years of age [2].

On the other hand, the pre-operative detection of frailty is becoming more relevant in these older surgical patients. Frailty has been shown to be a good predictor of post-operative complications of major gastrointestinal procedures [3], and it has been associated with post-operative mortality across all non-cardiac surgical specialties [4]. Additionally, frailty has a detrimental impact on costs and hospital profit for elective surgery [5]. Many reports suggest that frailty screening should be included in pre-operative assessments to enhance surgical decision-making and patient counseling [6–9].

In a systematic review regarding frailty in CRC surgical patients, Fagard et al. [10], found that only five quality articles with small numbers of patients and various definitions of frailty and post-operative outcomes, which made comparisons difficult. Recently, additional studies have been reported involving frail patients operated on for CRC, either in the elective setting [11, 12] or in the emergency setting [13], including a meta-analysis [14]. They also found that frailty is a robust predictor of severe post-operative complications in patients with colorectal cancer. However, the differences in long-term outcomes between frail and non-frail patients operated on for colorectal cancer have been less well documented. Furthermore, when assessing long-term results, in most of these studies, there is no adjustment for possible confounding factors related to the evolution of a neoplasm, such as tumor stage.

The aim of this study was to analyze the pre-, intra-, and post-operative differences in characteristics between older frail and non-frail patients with CRC and to investigate the long-term prognosis of these patients after adjusting for frailty, comorbidities, and tumor stage.

Methodology

Study design and participants

An observational study was conducted in a cohort of 149 consecutive patients older than 70 years old who underwent elective colorectal surgery for cancer between January 2013 and December 2015. Data were collected prospectively by a single surgeon and recorded in a database. The setting was a tertiary hospital that is responsible for a population of approximately 400,000 people. The study was approved by the Ethics Committee of the hospital (Code 140195). All patients consented to participate in the study.

Method

A surgeon and an anaesthesiologist pre-operatively evaluated all patients, and a complete anamnesis and physical examination were completed. The pre-operative geriatric assessment was performed by a specifically trained surgeon (MAA), regardless of the surgeon who operated on the patient. The geriatric evaluation usually lasted half an hour. The diagnosis of CRC was made by colonoscopy and biopsy. All patients underwent pre-operative thoraco-abdominal tomography to determine the extent of disease. Laboratory tests, electrocardiograms, and additional tests were also performed based on each patient's underlying condition. The anaesthesiologist did not normally refuse to administer anesthesia if the surgeon and family had agreed to undergo the procedure despite the presence of comorbidities or disabilities that were possible contraindications. In fact, there were no patients rejected for surgery, neither did any patient refuse surgery.

All the surgical procedures were performed by a staff surgeon, and reconstruction of the transit after resection was usually performed by mechanical anastomosis.

The cohort was divided into two groups: frail patients and non-frail patients.

The Clinical Frailty Score from the Canadian Study of Health and Aging (CSHA-CFS) was used to evaluate frailty in each patient. This instrument, which was proposed by Rockwood et al. [15], is based on a numerical

scale from 1 to 7 as follows: CFS 1 (very fit), CFS 2 (well), CFS 3 (well with treated comorbid disease), CFS 4 (apparently vulnerable), CFS 5 (mildly frail), CFS 6 (moderately frail), and CFS 7 (severely frail). We considered CSHA-CFS ≥ 4 as a threshold for determining frailty as it has been recently suggested that this cut-off highly correlates with postoperative outcomes [11].

The two groups were compared with regard to demographic data, comorbidities, functional and cognitive statuses, surgical risk, surgical variables, tumor extent, and post-operative outcomes, which were mortality at 30 days, 90 days, and 1 year after the procedure. All patients were followed for 5 years. Therefore, survival at 5 years was also recorded. No patients were lost to follow-up.

The following variables were evaluated:

Patient characteristics

Age and sex were recorded. Regarding the age cut-off point, the progressive increase in life expectancy in Western countries led us to consider it appropriate to include patients aged ≥70, which is 5 years older than the World Health Organization definition of the older population.

Preoperative status

Charlson Comorbidity Index (ChCI) The ChCI score was calculated pre-operatively for each patient. This score includes 19 medical conditions with assigned point values of 1, 2, 3, or 6, with totals ranging from 0 to 37 points. The absence of comorbidity is represented by 0 points; low levels of comorbidity are 1–2 points; moderate levels of comorbidity are 3–4 points; and high levels of comorbidity are > 4 points [16]. In this study, the ChCI was not adjusted for age or for the prevalence of AIDS [17], as there were no cases of this in the study population.

ASA (American Society of Anesthesiology) physical status classification system This scale was developed to offer clinicians a simple categorization of a patient's physiological status that could be helpful in predicting operative risk [18].

Functional status The functional status with regard to the basic activities of daily living (ADL) was determined using the Barthel Index [19]. The total score for this index ranges from 0, corresponding to a total dependence, to 100 points, corresponding to complete independence. For analytical purposes, this variable was categorized as independent (80–100 points) versus some grade of dependency (< 80 points) [20].

The previous functional status with regard to the Instrumental Activities of Daily Living (IADL) was also evaluated using the Lawton-Brody Index [21]. In summary, the score ranges from 0 (low function, dependent) to 8 points (high function, independent) for women and from 0 to 5 for men.

Cognitive status The Short Portable Mental State Questionnaire (SPMSQ) with the Pfeiffer test [22] was performed. This short questionnaire (10 items) provides an estimate of a patient's cognitive status according to the number of incorrect answers to basic questions, with values ranking from 0–1 (no impairment) to 9–10 (most severe impairment). In this study, the cut-off value was arbitrarily set at < 3 versus ≥ 3 errors.

Body Mass Index and Mini Nutritional Assessment Short Form questionnaire (MNA-SF) [23] The MNA-SF is a 6-item assessment tool based on the patient's body mass index (BMI), a dietary questionnaire and a subjective assessment. The maximum score is 14 points; the risk of malnutrition increases with decreasing scores.

Laboratory values The values of hemoglobin (gr/dL), serum creatinine (mg/dL), and serum albumin (gr/dL) were recorded.

Surgical variables The surgical variables were the type of surgical procedure performed, the use of a laparoscopic approach, the generation of an anastomosis (no/yes), and the need for at least one red blood cell unit transfusion during and/or immediately before or after the procedure (48 h).

Cancer stage (TNM) Tumor stage was recorded according to the 8th edition of the American Joint Committee on Cancer staging system and was categorized as stage I–II vs stage III–IV.

Post-operative complications Post-operative complications were graded using the Comprehensive Complication Index (CCI) [24]. This score summarizes all post-operative complications and seems to be more sensitive than other existing scales. The values of the index range from 0 (uneventful course) to 100 points (death). The Clavien-Dindo classification [25] was also used to assess the severity of post-operative complications. This variable was categorized into two categories: minor complications (grades I–II) and major complications (grades III–V).

Hospital stay The post-operative hospital stay of each patient was collected and registered.

Mortality Post-operative mortality, defined as any death within 30 days after the surgical procedure, 90-day mortality, and 1-year mortality after surgery, was also recorded.

Long-term survival All patients were followed for at least 5 years or until death. Their status was monitored through their medical history or telephone contact with either the patients themselves or their relatives. Long-term survival was considered as the period between the performance of the surgical procedure and death or the date of the last follow-up observation before the analysis, if the subject was still alive. The mean follow-up duration in the cohort was 5 years.

Statistical analysis

The data were analyzed using the statistical package SPSS 26.0 for Windows (IBM Corporation, Armonk, NY, USA). Categorical variables are summarized as frequencies and percentages; continuous variables are described as the means and standard deviations (SD) when the data followed a normal distribution or as medians and interquartile ranges (IQRs) when they did not. The Kolmogorov-Smirnov test was applied to evaluate the normality of the distribution of values in continuous variables.

Univariate analysis was performed to compare the characteristics of non-frail and frail patients with regard to pre-operative features, surgical variables, tumor extent, and post-operative outcomes.

The chi-squared test or Fisher's test was used to compare categorical data. For parametric distributions, Student's t test was used to compare the mean values of the two groups. For ordinal variables or non-parametric variables, the Mann–Whitney U test was used to compare the median values of the response variable.

Likewise, another univariate analysis was performed to compare the survival curves based on different independent variables. The survival curves were constructed using the Kaplan-Meier method. The log-rank test was applied to compare survival at 5 years.

Finally, multivariate Cox proportional hazards regression analysis was conducted. The primary purpose of the multivariate analysis was to adjust the variables habitually related to long-term survival (age, comorbidities, tumor stage) by the variable frailty, regardless of whether those variables were significant or not in the univariate analysis. Multicollinearity was tested using the variance inflation factor (VIF).

Statistical significance was defined as $p < 0.05$. The hazard ratio (HR) and 95% confidence interval (95% CI) were also calculated as measurements of associations using Cox regression.

Results

Out of the 149 patients, 96 (64.4%) were men and 53 (35.6%) were women, with a median age of 75 years (IQR 72–80). Only one patient was institutionalized. The rest of the patients lived at home with at least one relative and/or a caregiver.

According to the CSHA-CFS scale, 86 (57.7%) patients were grades 1–3; 44 (29.5%) patients were grades 4–5, and 19 (22.7%) were grades 6–7. After categorizing the variable (< 4 versus ≥ 4), 59 (39.6%), patients were considered frail, and 90 (60.4%) patients were not frail.

Pre-operative status

Forty-seven patients (31.5%) were classified as ASA I–II, and 102 (68.5%) were classified as ASA III–IV. The median ChCI score was 3.0 (IQR 2.0–4.0). Fourteen patients (9.4%) had a Barthel Index score < 80 points, and 135 (90.6%) had a Barthel Index score ≥ 80 points. The median value of the Lawton-Brody Index score was 6.0 (IQR 5.0–8.0). According to the Pfeiffer test, 140 (94%) patients had normal mental functioning, and 9 (6%) patients had cognitive impairment.

The mean body mass index was 26.8 kg/m^2 (SD ± 26.8). The median value of the MNA-SF test was 10.0 (IQR 9.0–12.0).

The mean level of hemoglobin was 12.5 g/dL (SD ± 2.2), the median level of serum creatinine was 0.96 mg/dL (IQR 0.79–1.13), and the mean level of serum albumin was 3.8 g/dL (SD ± 0.5).

Surgical variables

The following procedures were performed: right colectomy (70 patients), transverse colectomy (1 patient), left colectomy (12 patients), sigmoidectomy (17 patients), rectal anterior resection (33 patients), Hartmann procedure (3 patients), subtotal colectomy (3 patients), total colectomy (1 patient), abdominoperineal resection (8 patients), and resection of pelvic recurrence of rectal cancer (1 patient).

The laparoscopic approach was performed in 56 (38.9%) procedures, and anastomosis was carried out in 127 (85.2%) patients.

Peri-operatively, 33 (22.1%) patients received at least one red blood transfusion.

Tumor extent

In 45 (30.2%) patients, the tumor did not extend past the muscularis propria layer (T1–T2), and in 104 (69.8%) patients, the tumor invaded through the muscularis propria into peri-colorectal tissues or penetrated the visceral peritoneum or other organs (T3–T4). Likewise, 102 (68.5%) patients did not have lymph node involvement (N0), and 47 (31.5%) had lymph node

involvement (N1). Only 7 (4.7%) patients had distant metastasis (M1).

According to the 8th edition of the American Joint Committee on Cancer Staging, 99 (66.4%) patients were classified as having TNM stage I–II disease, and 50 (33.6%) patients were classified as having stage III–IV disease.

Of the 7 patients with distant metastases at diagnosis, only 2 patients underwent curative surgery (liver metastasectomy). In the other 5 patients, resection of the primary tumor was performed on a palliative basis because the neoplasm was highly symptomatic.

Post-operative complications

Seventy-four patients (49.7%) had at least 1 post-operative complication, of whom 42 (28.25%) patients were classified as Clavien–Dindo grades I–II (minor complications), and 32 (21.5%) patients grades III–V (major complications), including 5 deaths. The median Comprehensive Complication Index score was only 8.7 (IQR 0.0–24.2). Within the group of patients who had complications (CCI ≥ 1), the median CCI score was 33.3 (IQR 8.7–46.3). Anastomosis dehiscence was observed in 10 patients (7.9% of the patients with anastomosis).

Outcomes

The median post-operative hospital stay was 10 days (IQR 7–15). Hospital stay was associated with the severity of complications ($p < 0.001$). The median hospital stay of the patients without complications was 7 days (IQR 6.0–9.0), while the median hospital stay of the patients with minor complications was 13 days (IQR 9.0–16.0), and the median hospital stay of the patients with major complications was 26 days (IQR 15.0–38.5).

The operative mortality rate (30 days) was 3.4% (5 patients). The causes of death were anastomotic dehiscence (2 patients), cardiogenic shock (1 patient), pneumonia (1 patient), and venous mesenteric ischemia due to massive venous thrombosis (1 patient).

The 90-day mortality rate was 8.1% (12 patients), and the 1-year mortality rate was 12.8% (19 patients).

By the end of the follow-up period, 48 (17.6%) patients had died. The cumulative survival rates at 3 and 5 years were 78.4% and 68%, respectively. Out of the 43 patients who died during follow-up, 21 (48.8%) patients died due to tumor progression, and 22 (51.2%) patients died due to non-tumor-related causes.

Regarding chemotherapy, only 37 (24.8%) patients received neo- or adjuvant chemotherapy. In 10 (6.7%) cases, it was administered as neoadjuvant therapy. The patients in whom chemotherapy was not administered were mainly due to comorbidity or an advanced degree of frailty.

The results of the comparisons between frail and non-frail patients are summarized in Table 1. Frail patients were significantly older, were more likely to have impaired cognition, and had a worse functional status, more comorbidities, a higher operative mortality rate, and more serious complications than non-frail patients. However, there were no significant differences in mortality between these two groups at 90 days and 1 year after the surgical procedure. Furthermore, although a smaller proportion of the frail patients than the non-frail patients were alive at 5 years, the survival analysis did not show statistically significant difference between the two groups. The mean survival time in frail patients was 58.9 months, whereas non-frail patients had a mean survival of 63.9 months ($p = 0.246$) (Fig. 1).

Univariate analyses of the factors related to long-term survival are summarized in Table 2. Comorbidities, as measured by the Charlson Comorbidity Index ($p = 0.001$); the Lawton-Brody Index ($p = 0.011$); failure to perform an anastomosis ($p = 0.024$); nodal involvement ($p = 0.005$); distant metastases ($p < 0.001$); high TNM stage ($p = 0.004$); and anastomosis dehiscence ($p = 0.013$) were significant univariate predictors of a poor prognosis.

Multivariate analysis of long-term survival, with adjustment for age, frailty, comorbidities, and TNM stage, showed that comorbidities ($p = 0.002$; HR 1.30; 95% CI 1.10–1.54) and TNM stage ($p = 0.014$; HR 2.06–95% CI 1.16–3.67) were the only independent risk factors for survival at 5 years (Table 3). No multicollinearity was detected among the independent variables.

Discussion

This study showed that frail patients were significantly older, were more likely to have impaired cognition, and had a worse functional status, more comorbidities, a higher operative mortality rate, and more serious complications than non-frail patients. These findings, which are related to early outcomes, are in line with what has recently been published in relation to pre-operative frailty [10].

In recent years, there has been an emphasis on the fact that a lack of adequate physiological reserves affects the survival of older patients undergoing surgical procedures. Frailty has been defined as a multifactorial syndrome characterized by decreased reserves and less resistance to stressors, resulting from a cumulative decline across multiple physiological systems and the subsequent vulnerability to adverse outcomes [26]. This concept was previously applied, in general, only to non-surgical patients, and there is still no clear consensus regarding its application to elderly surgical patients [27]. Nonetheless, frailty has become an emerging risk

Table 1 Comparative analysis between frail and non-frail patients with CRC, according to the CSHA-CSF scale

Variable	Total *N* (%) 149 (100)	No frailty *N* (%) 90 (60.4%)	Frailty *N* (%) 59 (39.6%)	*P*
Age				
Median (IQR)	75 (72–80)	74 (72–29)	77 (73–81)	0.008*
Gender				
Men	96 (64.4)	61 (67.8)	35 (59.3)	0.292
Women	53 (35.6)	29 (32.2)	24 (40.7)	
ASA				
I–II	47 (31.5)	32 (35.6)	15 (25.4)	0.193
III–IV	102 (68.5)	58 (64.4)	44 (74.6)	
Charlson Index				
Median (IQR)	3.0 (2.0–4.0)	2.0 (2.0–4.0)	3.0 (2.0–4.0)	0.005*
Barthel				
< 80	14 (9.4)	1 (1.1)	13 (22.0)	< 0.001*
≥ 80	135 (90.6)	89 (98.9)	46 (78.0)	
Lawton-Brody				
Median (IQR)	6.0 (5.0–8.0)	7.0 (6.0–8.0)	4.0 (3.0–6.0)	< 0.001*
Pfeiffer				
< 3	140 (94.0)	89 (98.9)	51 (86.4)	0.003*
≥ 3	9 (6.0)	1 (1.1)	8 (13.6)	
BMI[a]				
Mean ± SD	26.8 (± 4.0)	26.9 (± 4.2)	26.5 (± 3.7)	0.746
MNA[b]				
Median–IQR	10.0 (9.0–12.0)	11.0 (9.0–13.0)	10.0 (9.0–12.0)	0.185
Hemoglobin gr/dL				
Mean (±SD)	12.5 (± 2.2)	12.6 (± 2.1)	12.3 (± 2.2)	0.507
Creatinine mg/dL				
Median (IQR)	0.96 (0.79–1.13)	0.96 (0.82–1.06)	0.97 (0.75–1.22)	0.840
Albumin gr/dL				
Mean (±SD)	3.8 (± 0.5)	3.8 (± 0.5)	3.8 (± 0.5)	0.963
Laparoscopic approach				
n (%)	56 (38.9)	30 (53.6)	26 (46.4)	0.230
Anastomosis				
No	22 (14.8)	13 (14.4)	9 (15.3)	0.892
Yes	127 (85.2)	77 (85.6)	50 (84.7)	
Transfusions				
No	116 (77.9)	71 (78.9)	45 (76.3)	0.707
Yes	33 (22.1)	19 (21.1)	14 (23.7)	
T				
1–2	45 (30.2)	25 (27.8)	20 (33.9)	0.426
3–4	104 (69.8)	65 (72.2)	39 (66.1)	
N				
0	102 (68.5)	60 (66.7)	42 (71.2)	0.561
1	47 (31.5)	30 (33.3)	17 (28.8)	
M				
0	142 (95.3)	87 (96.7)	55 (93.2)	0.436

Table 1 Comparative analysis between frail and non-frail patients with CRC, according to the CSHA-CSF scale *(Continued)*

Variable	Total *N* (%) 149 (100)	No frailty *N* (%) 90 (60.4%)	Frailty *N* (%) 59 (39.6%)	*P*
1	7 (4.7)	3 (3.3)	4 (6.8)	
TNM stage				
I–II	99 (66.4)	59 (65.6)	40 (67.8)	0.777
III–IV	50 (33.6)	31 (34.4)	19 (32.2)	
Anastomosis dehiscence				
No	139 (93.3)	86 (95.6)	53 (89.8)	0.195
Yes	10 (6.7)	4 (4.4)	6 (10.2)	
CCI ≥ 1[c]				
Median (IQR)	33.3 (8.7–46.3)	21.8 (8.7–41.3)	32.4 (20.9–55.4)	0.04*
Hospital stay				
Median (IQR)	10 (7–15)	10 (7–16)	9 (7–15)	0.259
Chemotherapy				
No	112 (75.2)	60 (66.7)	52 (88.1)	0.003*
Yes	37 (24.8)	30 (33.3)	7 (11.9)	
30-day mortality				
No	144 (96.6)	90 (100.0)	54 (91.5)	0.009*
Yes	5 (3.4%)	0 (0.0)	5 (8.5)	
90-day mortality				
No	137 (91.9)	85 (94.4)	52 (88.1)	0.166
Yes	12 (8.1)	5 (5.6)	7 (11.9)	
1-year mortality				
No	130 (87.2)	80 (88.9)	50 (84.7)	0.458
Yes	19 (12.8)	10 (11.1)	9 (15.3)	
Cumulative survival at 5 years				
(mean months)	62.16	63.9	58.9	0.246
Death from non-tumoral causes				
n (%)	21 (43.8)	11 (42.3)	16 (72.7)	0.034*

[a]*BMI* body mass index
[b]*MNA* Mini-Nutritional-Assessment
[c]*CCI* Comprehensive complication index
*Statistically significant

stratification measure in surgical risk patients and may also be a valuable quality metric [12].

Therefore, for many authors, an assessment of frailty is essential for estimating the overall and functional outcomes in geriatric surgical patients, depending on the planned intervention [28].

For this purpose, the pre-operative performance of the process called the comprehensive geriatric assessment (CGA) is recommended. Ellis et al. [29] defined CGA as a multidimensional diagnostic and therapeutic process that is focused on determining a frail older person's medical, functional, mental, and social capabilities and limitations with the goal of ensuring that problems are identified, quantified, and managed appropriately. The International Society of Geriatric Oncology has recommended the use of the CGA to guide the development of an oncologic treatment plan in older patients with cancer, including those who need to undergo surgery [30]. Nevertheless, there is also a current trend to use previously defined and highly useful frailty scales to detect this deficiency, such as the CSHA-CFS score [15] or the different versions of the Modified Frailty Index of the American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) [12, 31].

Focusing on colorectal cancer surgery, two systematic reviews [10, 14] also reported the same conclusions: frailty is a good predictor of post-operative complications after elective colorectal surgery. Therefore, assessing frailty in colorectal oncology seems important to determining the operative risks and benefits and to

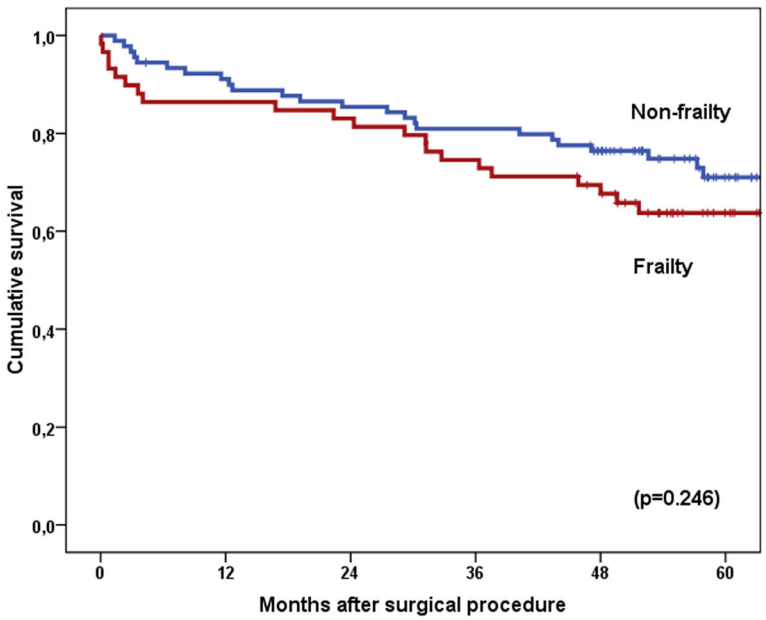

Fig. 1 Differences in cumulative survival between non-frail and frail patients. Log-rank test ($p = 0.246$)

guiding peri-operative management. However, the relationship between frailty and long-term survival has not been well studied [10, 31]. Most studies report 30-day mortality [13, 14, 31–34], 3-month mortality [35], and 1-year mortality as output variables [35]. Few studies [36] have provided a follow-up of this population at 5 years. Furthermore, the variable "frailty" in these reports is not usually adjusted for possible confounders such as age, comorbidities and tumor stage. Only Ommundsen et al. [36] reported the results of a multivariable analysis adjusting frailty for TNM stage, age, and sex in older patients operated on for CRC; however, there was no adjustment for comorbidities. These authors studied 1-year and 5-year survival rates in this population. The comparison between frail and non-frail older patients showed survival rates of 80% and 92%, respectively, for 1-year survival and 24% and 66%, respectively, for 5-year survival. They concluded that the impact of frailty on 5-year survival is comparable with that of TNM stage after CRC surgery. These results differ from those obtained in our series. We observed that the long-term survival of frail patients operated on for colorectal cancer was fundamentally related to comorbidities and tumor stage. Therefore, although operative mortality is higher in frail patients than in non-frail patients, frailty per se does not seem to be a determining factor for the long-term survival of these patients, even after adjustment for comorbidities and tumor stage. Only one study [35] reached the same conclusions, but that study included a small number of patients and a follow-up period of only 1 year.

The observed differences could be explained if we consider three points of discussion.

First, the definition of the concept of frailty and the method used to assess frailty were different. Although the published literature includes several scales for defining frailty in surgical patients, there is no single gold standard measure for frailty in this context. Multiple frailty screening tools have been developed [8, 37], and their usefulness is somewhat variable among different patient populations, indications for surgery, and surgical procedures performed. The overwhelming number of risk scales developed, most of which have been applied to small populations, has led to few being used consistently in clinical practice.

In our series, the CSHA-CFS was used to determine frailty. It is simple to administer and correlates well with the frailty index, which has been shown to predict morbidity and mortality in some surgical populations [38]. Although this study did not aim to compare the CSHA-CFS with other frailty scales, the CSHA-CFS has certain advantages, such as being less time-consuming, having been validated, and being easy to perform [38]; in addition, it has very good inter-rater reliability [39]. The proportion of patients with frailty in our study was 40%, which is comparable to the proportions reported in the previously published literature (25–46%) [27].

The ACS-NSQIP 11-item Modified Frailty Index (11-mFI) [12], the ACS-NSQIP 5-item Modified Frailty Index (5-mFI) [13, 31], both based on the CSHA scale; the Fried criteria [26, 33]; the Groningen Frailty Indicator [34, 40]; and a series of cut-offs for the components

Table 2 Univariate analysis of long-term survival using Cox regression for each variable

Variables	Total *N* (%) 149 (100)	Alive 101 (67.8%)	Death 48 (32.2%)	*P*	HR (CI 95%)
Age					
Median (IQR)	75 (72–80)	74 (72–79)	78 (73–80.75)	0.140	1.03 (0.99–1.09)
Gender					
Men	96 (64.4)	61 (60.4)	35 (72.9)	0.074	0.56 (0.30–1.07)
Women	53 (35.6)	40 (39.6)	13 (27.1)		
ASA					
I–II	47 (31.5)	36 (35.6)	11 (22.9)	0.241	1.50 (0.76–2.94)
III–IV	102 (68.5)	65 (64.4)	37 (77.1)		
Charlson Index					
Median (IQR)	3.0 (2.0–4.0)	3.0 (2.0–3.0)	3.0 (2.0–5.0)	0.001*	1.37 (1.17–1.60)
Barthel					
< 80	14 (9.4)	8 (7.9)	6 (12.5)	0.314	0.64 (0.27–1.52)
≥ 80	135 (90.6)	93 (92.1)	42 (87.5)		
Lawton-Brody					
Median (IQR)	6.0 (5.0–8.0)	7.0 (5.0–8.0)	6.0 (4.0–7.0)	0.011*	0.85 (0.76–0.97)
Pfeiffer					
< 3	140 (94.0)	97 (96.0)	43 (89.6)	0.157	1.95 (0.77–4.94)
≥ 3	9 (6.0)	4 (4.0)	5 (55.6)		
BMI[a]					
Mean ± SD	26.8 (± 4.0)	26.7 (± 4.1)	26.9 (± 3.7)	0.938	1.00 (0.94–1.07)
MNA[b]					
Median IQR	10.0 (9.0–12.0)	10.0 (9.0–12.5)	10.5 (9.0–12.0	0.588	0.97 (0.85–1.09)
Frailty					
No	90(60.4)	64 (63.4)	26 (54.2)	0.249	1.40 (0.79–2.47)
Yes	59 (39.6)	37 (36.6)	22 (45.8)		
Hemoglobin gr/dL					
Mean (±SD)	12.5 (± 2.2)	12.6 (± 2.1)	12.3 (± 2.3)	0.703	0.98 (0.86–1.11)
Creatinine mg/dL					
Median (IQR)	0.96 (0.79–1.13)	0.94 (0.79–1.07)	1.00 (0.80–1.33)	0.060	1.66 (0.98–2.81)
Albumin gr/dL					
Mean (±SD)	3.8 (± 0.5)	3.8 (± 0.5)	3.7 (± 0.5)	0.430	0.749 (0.37–1.54)
Laparoscopic approach					
n (%)	56 (38.9)	41 (40.6)	15 (31.3)	0.118	0.635 (0.36–1.12)
Anastomosis					
No	22 (14.8)	10 (9.9)	12 (25.0)	0.024*	0.47 (0.24–0.91)
Yes	127 (85.2)	91 (90.1)	36 (75.0)		
Transfusions					
No	116 (77.9)	80 (79.2)	36 (75.0)	0.516	1.24 (0.65–2.39)
Yes	33 (22.1)	21 (20.8)	12 (25.0)		
T					
1–2	45 (30.2)	34 (33.7)	11 (22.9)	0.228	1.51 (0.77–2.97)
3–4	104 (69.8)	67 (66.3)	37 (77.1)		
N					
0	102 (68.5)	76 (75.2)	26 (25.5)	0.005*	2.27 (1.29–4.01)

Table 2 Univariate analysis of long-term survival using Cox regression for each variable *(Continued)*

Variables	Total *N* (%) 149 (100)	Alive 101 (67.8%)	Death 48 (32.2%)	*P*	HR (CI 95%)
1	47 (31.5)	25 (24.8)	22 (45.8)		
M					
0	142 (95.3)	100 (99.0)	42 (87.5)	< 0.001*	6.21 (2.59–14.93)
1	7 (4.7)	1 (1.0)	6 (12.5)		
TNM stage					
I–II	99 (66.4)	74 (73.3)	25 (52.1)	0.004*	2.29 (1.30–4.04)
III–IV	50 (33.6)	27 (26.7)	23 (15.4)		
Anastomosis dehiscence					
No	139 (93.3)	97 (96.0)	42 (87.5)	0.013*	2.95 (1.25–6.96)
Yes	10 (6.7)	4 (4.0)	6 (12.5)		
Chemotherapy					
No	112 (75.2)	75 (74.3)	37 (77.1)	0.890	0.95 (0.49–1.87)
Yes	37 (24.8)	26 (25.7)	11 (22.9)		

[a]*BMI* body mass index
[b]*MNA* Mini-Nutritional-Assessment
*Statistically significant

of the pre-operative geriatric assessment [35, 36], have been used to detect frailty by other authors.

Therefore, given the large number of scales used, it is difficult to make comparisons between the series analyzed.

Second, there was confusion between frailty and comorbidities in some of the previously described frailty rating scales. The components of the pre-operative geriatric assessment with cut-off values for frailty used by some authors [35, 36], the 11-mFI [12] and 5-mFI [13, 31] scores mix up, in the same scale, comorbidities with other values used to define frailty. Actually, the terms "frailty," "disability," and "comorbidity" may be considered somewhat confusing concepts in older surgical patients. According to Richard et al. [41], there is an overlap of these concepts that may determine the systematic evaluation of the three concepts in all patients. Specifically, frailty and comorbidities are prevalent in older adults and are strongly interrelated. Previously, comorbidities were even considered to be a component of frailty [14]. However, we agree with Fried et al. [26] that frailty may have a biologic basis and be a distinct clinical syndrome. We believe that it is important to distinguish comorbidities from frailty, and it might be appropriate to assess them separately. A patient may have comorbidities and may not be considered frail, and a frail patient may not necessarily have comorbidities. To avoid this bias, in our study, we used the CSHA to define frailty and analyzed comorbidities and disability independently.

Third, the heterogeneity of the studied sample is an important consideration. We included in our series only patients undergoing elective surgery for colorectal cancer. However, other reported series [12, 31] have included patients who underwent any elective or non-elective colorectal procedures. Simon et al. [13] focused on emergency colorectal surgery and showed that frailty is associated with morbidity, mortality, and loss of independence in older patients.

Therefore, previously published data regarding the relationship of frailty with long-term mortality in patients with colorectal cancer should be analyzed with caution.

According to the results obtained, we found that comorbidities prior to intervention and tumor stage are the two strongest predictors of long-term survival in geriatric patients with colorectal cancer. Boakye et al. [14] concluded that comorbidities and frailty are strong predictors of survival in CRC patients but did not adjust for these variables and had a short follow-up duration.

Table 3 Multivariate analysis (Cox regression) of long-term survival, adjusting for age, frailty, comorbidity, and TNM stage

Variables	*B*	SE	Wald	*p*	HR (95.0% CI)
Age	0.028	0.026	1.229	0.268	1.03 (0.98–1.08)
TNM stage	0.723	0.295	5.999	0.014*	2.06 (1.16–3.67)
Charlson Comorbidity Index	0.263	0.085	9.496	0.002*	1.30 (1.10–1.54)
Frailty	0.044	0.315	0.019	0.889	1.05 (0.56–1.94)

*Statistically significant. *B* regression coefficient, *CI* confidence interval, *HR* hazard ratio, *SE* standard error, *Wald* test statistic

The possible mechanisms by which comorbidities might affect the prognosis of patients with colorectal cancer have been well documented by these authors. As we observed in our results, there does not seem to be an association between comorbidities and CRC stage at diagnosis. However, comorbidities might independently increase the risk of non-cancer-related deaths. These patients might also have disabilities and worse post-operative outcomes, which could negatively affect their long-term prognosis. Moreover, these patients are less likely to receive standard cancer treatments such as chemotherapy. Comorbidities may also interact with CRC, affecting tumor biology, accelerating disease progression or increasing the risk of mortality [14].

However, tumor stage at diagnosis is by far the most important factor and is the main consideration with regard to treatment recommendations in CRC care guidelines [42]. In our analysis, the effect of tumor stage on long-term survival was very strong and was comparable to the effect of comorbidities. Age, sex, and other predictive variables, such as nutritional status, were not related to long-term survival in our sample.

Knowledge of these factors in this population may help us appropriately advise the patient and their family during the pre-operative decision-making process. This does not mean that we should simply reject the possibility of surgery in frail patients with comorbidities and advanced cancer stages. A potential modification of the syndrome well in advance of potential surgery may also be included in the benefits of frailty assessment: pharmacological interventions, nutritional supplementation, prehabilitation exercise programmes, etc. [43]. These subjects have not been addressed in this study.

Another important factor to consider here is the quality of life secondary to sustained functional decline, which is common after colon cancer surgery [44]. Reducing the remaining quality of life in these patients would not make sense. This topic was not studied in this report either. Therefore, the decision must be made individually with all the information available on the expected survival and the post-operative quality of life in an attempt to avoid overtreatment or undertreatment, two well-known pitfalls in geriatric oncology [36].

The present study has several limitations. This was a single-center study, and we wondered if a larger sample size would reveal additional variables that were predictive of long-term mortality in the univariate analysis. However, although data were collected prospectively, there was a long follow-up period, and consecutive subject inclusion, in which all of the patients agreed to participate, there may have been a selection bias prior to the referral of each case. It would be interesting to know the median CFS score of patients excluded from surgery before submission to the surgical setting, in comparison to the patients included into the study to shed some light on selection bias, but these data could not be collected. This study also has significant strengths, such as the homogeneity of the sample. All of our patients were treated for colorectal cancer with elective surgery, and the long-term mortality was comparable to that published in other series [45]. A standardized pre-operative geriatric assessment was performed in all the patients in the same pre-operative setting in a truly older population. Therefore, unlike other recently published studies with heterogeneous populations, we consider that the results obtained in this study could be generalized more specifically to the population of older patients with colorectal cancer.

Concerning other factors that could also have influenced the results, it has been suggested that ERAS pathways and minimal invasive surgical technique may play an important role in the successful outcome in older patients after colorectal surgery. In our series, no multimodal rehabilitation protocol was implemented in these old patients. We believe in the benefits of these programs that we are currently applying, but in a recent published trial, Carli et al. [46] concluded that prehabilitation does not seem to improve postoperative outcomes compared with postoperative rehabilitation in frail patients undergoing colorectal cancer resection.

As to laparoscopic surgery, this approach is considered superior to open surgery for frail patients undergoing colon resection. It has been demonstrated that increases in frailty magnify differences between approaches [47]. The rate of intervention performed laparoscopically in our patients was relatively low since during the study period this approach was still being implemented. However, there were no differences in the number of laparoscopic procedures performed between frail and no frail patients, and we found no significant differences in long-term survival depending on the type of approach.

In conclusion, frailty assessed with CSHA-CFS scale is associated with poor short-term post-operative outcomes, but it does not seem to affect long-term survival in patients with colorectal cancer. Instead, high Charlson Comorbidity Index and tumor stage are good predictors of long-term survival. More large-scale studies with adjustment for more prognostic factors are needed. Therefore, frailty should not be considered a contraindication for adequate planning of colorectal cancer treatment in older patients, but it should be individualized taking into account comorbidity and tumor stage rather than frailty itself.

Abbreviations

ACS-NSQIP: American College of Surgeons National Surgical Quality Improvement Program; ADL: Activities of daily living; ASA: American Society of Anesthesiology; CCI: Comprehensive Complication Index; CGA: Comprehensive Geriatric Assessment; ChCI: Charlson Comorbidity

Index; CI: Confidence interval; CRC: Colorectal cancer; CSHA-CFS: Aging-Clinical Frailty Scale; HR: `Hazard ratio; IQR: Interquartile range; MNA-SF: Mini Nutritional Assessment Short Form questionnaire; SD: Standard deviation; SPMSQ: Short Portable Mental State Questionnaire

Acknowledgements
Not applicable

Authors' contributions
MAA: data collection, contributed to writing the manuscript. CRC: data collection, contributed to writing the manuscript. RFC: data collection, contributed to writing the manuscript. ACM: data analysis, corrected the manuscript. MAAM: corrected the manuscript. JMG: design, statistical analysis, and coordination. The authors read, commented, and approved the manuscript.

Funding
Not applicable

Availability of data and materials
Not applicable

Declarations

Ethics approval and consent to participate
The study was approved by the Hospital Ethics Committee (Code 120273).

Consent for publication
Not applicable

Competing interests
The authors declare that they have no competing interests.

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Received: 26 January 2021 Accepted: 31 March 2021
Published online: 10 April 2021

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Publisher's Note

CONCLUSIONES

A la vista de los resultados obtenidos tras el desarrollo de esta investigación, podemos concluir que:

1. A los pacientes ancianos, incluida la población de nonagenarios, se les puede ofrecer un tratamiento quirúrgico curativo oncológico. La cirugía con intención radical en pacientes nonagenarios afectos por cáncer colorrectal, es relativamente segura y puede lograr una adecuada supervivencia a largo plazo. La edad avanzada, per se, no es una enfermedad y nunca debe ser una contraindicación para un procedimiento quirúrgico en pacientes con cáncer colorrectal. Además, queda de manifiesto que la edad cronológica sirve como un pobre sustituto de la edad biológica, que en sí misma es difícil de definir o determinar.
2. El grado de fragilidad determinado mediante la escala CSHA-CFS (Canadian Study of Health and Aging Clinical Frailty Scale) se correlaciona estrechamente con el desarrollo de complicaciones postoperatorias inmediatas según el CCI (Comprehensive Complication Index). Es, por tanto, un buen predictor de complicaciones posoperatorias en los pacientes de edad avanzada que se someten a procedimientos gastrointestinales mayores.

   3. La fragilidad evaluada con la escala CSHA-CFS se asocia con malos resultados posoperatorios a corto plazo, pero no parece afectar a la supervivencia a largo plazo en pacientes con cáncer colorrectal. En cambio, tanto el Índice de Comorbilidad de Charlson elevado, como el estadio tumoral, son buenos predictores de supervivencia a largo plazo. Por lo tanto, la fragilidad no debe

considerarse una contraindicación para la planificación adecuada del tratamiento del cáncer colorrectal en pacientes mayores, sino que debe individualizarse teniendo en cuenta la comorbilidad y el estadio del tumoral.

RESUMEN

El envejecimiento implica una mayor tasa de trastornos crónicos, muchos de los cuales cuentan con la opción quirúrgica en su plan terapéutico.

El Cáncer Colorrectal (CCR) es la tercera neoplasia más frecuente de forma global y afecta a aproximadamente el 60% de los pacientes con edades iguales o superiores a 70 años.

Conocer las características preoperatorias de la población mayor sometida a procedimientos quirúrgicos gastrointestinales, así como cribar la fragilidad preoperatoria, va a permitir predecir el desarrollo de complicaciones postoperatorias, su supervivencia, facilitar el asesoramiento médico y reducir los costes sanitarios.

La edad avanzada no es una enfermedad y nunca debe ser una contraindicación para un procedimiento quirúrgico en pacientes con CCR, incluso en pacientes nonagenarios.

La fragilidad determinada mediante la escala Clinical Frailty Scale, es un buen predictor de complicaciones posoperatorias inmediatas en los pacientes mayores sometidos a procedimientos gastrointestinales, sin embargo, no debe considerarse una contraindicación para la cirugía radical del CCR, debiendo tenerse en cuenta la comorbilidad previa y el estadio del tumoral.

PALABRAS CLAVES

Adulto mayor, cáncer colorrectal, cirugía gastrointestinal, fragilidad, mortalidad, nonagenarios, supervivencia a largo plazo, complicaciones postoperatorias, valoración geriátrica.

SUMMARY

Aging implies a higher rate of chronic disorders, many of which have the surgical option in their treatment plan.

Colorectal Cancer (CRC) is the third most frequent neoplasm globally and affects approximately 60% of patients aged 70 years or older.

To know the preoperative characteristics of the elderly population undergoing gastrointestinal surgical procedures, as well as screening for preoperative frailty, will allow predicting the development of postoperative complications, their survival, facilitating medical advice and reducing healthcare costs.

Advanced age is not a disease and should never be a contraindication for a surgical procedure in patients with CRC, even in nonagenarians.

Frailty, determined by the Clinical Frailty Scale, is a good predictor of postoperative complications in elderly patients undergoing major gastrointestinal procedures. However, it should not be considered a contraindication for radical CRC surgery in older patients, considering previous comorbidity and tumor stage.

KEYWORDS:

Colorectal cancer, geriatric assessment, frailty, gastrointestinal surgery, long-term survival, mortality, nonagenarians, older adult, post-operative outcome.