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UNIDAD ACADÉMICA DE CIENCIAS QUÍMICAS Y DE LA SALUD

CARRERA DE CIENCIAS MÉDICAS

ESTRATIFICACION Y MANEJO TERAPÉUTICO DEL SÍNDROME CORONARIO AGUDO SIN ELEVACIÓN DEL SEGMENTO ST

MENDOZA BASURTO GISSELLA DEL CISNE
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EXAMEN COMPLEXIVO

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CHU LEE ANGEL JOSE

MACHALA, 04 DE FEBRERO DE 2019

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04 de febrero de 2019

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RESUMEN

Objetivo: determinar la evaluación rápida mediante estratificación de riesgo y el manejo concreto del síndrome coronario agudo sin elevación del segmento ST, con el fin de establecer la causa del aumento de la morbimortalidad a nivel hospitalaria.

Materiales y métodos: para llevar al cabo este proceso investigativo, se realizó la revisión de 18 artículos científicos de la mejor evidencia, obtenidos de revistas indexadas, conjuntamente se incluyó 2 guías clínicas europea y Americana. Del material en estudio se realizó una síntesis con el fin de destacar la terapéutica adecuada con la evidencia 1A, respecto a la atención del paciente con síndrome coronario agudo sin elevación del segmento ST.

Resultados: de las 20 bibliografías en estudio se obtuvo los siguientes resultados, la estratificación de riesgo TIMI/GRACE son puntos claves para el manejo del paciente, en cuanto a este se considera la Angiografía coronaria como el Gold estándar y posteriormente el tratamiento farmacológico que incluye los anti isquémicos, anticoagulantes, anti plaquetarios y las estatinas, posteriormente corrección de los factores de riesgo modificables.

Conclusiones: las pautas clínicas y terapéuticas para el tratamiento adecuado del paciente están descritas en la literatura, con los suficientes estudios que corroboran la información, sin embargo la falta de recursos en países subdesarrollados y la falta de adherencia al tratamiento, llevan al aumento de la morbimortalidad y el deterioro de la calidad de vida.

Palabras claves: evaluación, estratificación, factores de riesgo, tratamiento, mortalidad.

ABSTRACT

Objective: to determine the rapid assessment by risk stratification and the management of acute coronary syndrome without ST segment increase, in order to establish the cause of the increase in morbidity and mortality at the hospital level.

Materials and methods: to carry out this investigative process, a review was made of 18 articles of the best evidence, the results of the indexed journals, 2 European and American clinical guidelines were included. The material in the study was carried out a synthesis in order to highlight the appropriate therapy with evidence 1A, respect for the care of the patient with acute coronary syndrome without ST segment grade.

Results: the 20 bibliographies in the study obtained the following results, the TIMI / GRACE risk stratification are some of the keys for the patient's management, and also the coronary angiography as the standard gold and the pharmacological treatment that includes anti ischemic , anticoagulants, antiplatelet agents and statins, later modifiable risk factors are corrected.

Conclusions: the clinical and therapeutic guidelines for the adequate management for the patient are described in the literature, with sufficient studies that corroborate the information, however the lack of resources in the underdeveloped countries and the lack of adherence to the treatment, lead to the increase of the mortality and the deterioration of the quality of life.

Keywords: Evaluation, stratification, risk factors, treatment, mortality.

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INTRODUCCION

El presente trabajo de revisión bibliográfica, con aborde científico refiere al tema del Síndrome coronario agudo sin elevación del segmento ST, el cual presenta una alta mortalidad durante los últimos años, por lo cual se ha considerado oportuna la revisión de artículos científicos de revistas indexadas para determinar el mejor abordaje terapéutico para el paciente.

El síndrome coronario agudo es una emergencia médica, atribuida a la presencia de factores de riesgo los cuales originan la ruptura de placas de ateroma y consiguiente obstrucción de la circulación haciendo referencia a los síntomas clínicos.

La investigación de esta problemática se basa en el manejo del paciente en cuanto al tratamiento adecuado y el uso de escalas para la estratificación (TIMI / GRACE) en cuanto al riesgo isquémico, y por otro lado la infraestructura y falta de recursos en países subdesarrollados como el nuestro para la aplicación de la Angioplastia y estudios hemodinámicos a todos los pacientes que según las guías es considerado el Gold Estándar en cuanto al tratamiento.

En el desarrollo este contexto se incluyó la revisión de meta análisis y ensayos clínicos controlados, aleatorizados, con la mejor evidencia científica en su mayoría clase 1A, además de las Guías Clínicas tanto Europea como Americana del manejo del paciente con síndrome coronario agudo, está fundamentada en artículos científicos de la mejor evidencia que son de alto impacto, por lo cual fueron utilizadas como herramientas claves para el progreso de este trabajo ya mencionado.

1. DESARROLLO

El Síndrome Coronario agudo es un término muy amplio el cual abarca diferentes situaciones de afección Cardiaca y circulatoria. (1) Según la interpretación electrocardiográfica y semiológica se clasifica en:

Síndrome coronario agudo sin elevación del segmento ST

Síndrome coronario agudo con elevación del segmento ST

Muerte súbita

De acuerdo a las Guías Europeas de Cardiología, se considera de vital importancia la realización de un Electrocardiograma dentro de los 10 primeros minutos de haber recibido al paciente en el área de emergencia con evidencia de patología cardiaca. (2) (3)

1.1 SINDROME CORONARIO AGUDO SIN ELEVACION DEL SEGMENTO ST

1.1.1. Definición

El síndrome coronario agudo sin elevación del segmento ST, incluye; angina inestable y el Infarto agudo de miocardio. (1) Ambos describen el dolor precordial típico de aproximadamente 20 minutos de duración que aparece tras el esfuerzo físico y sede en el reposo. (3) Se adjuntó recientemente una cuarta definición dada por la Sociedad Europea de Cardiología conocida como daño miocárdico, el cual describe valores elevados de Troponina cardiaca con un valor por encima del percentil 99, esto se traduce en isquemia miocárdica. (1)

1.1.2 Epidemiologia

El síndrome coronario agudo per se, es descrito como una de las causas más trascendentes de emergencias médicas a nivel hospitalario, y por ende una de las principales causas de muerte a nivel mundial (2)(1)

En el estudio retrospectivo denominado (**RESCATA-SEST)**; se considera que del seguimiento de 286 pacientes hospitalizados con diagnóstico de Síndrome coronario

agudo sin elevación del segmento ST, un número considerable de 178 pacientes que padecieron esta patología fueron hombres, con una edad promedio de 60 años y destacándose los principales factores de riesgo cardiovascular, la Hipertensión arterial, dislipidemia y sedentarismo. (4)

1.1.3 Fisiopatología

El desarrollo fisiopatológico, presenta un factor denominador, conocido como placa de ateroma localizado a nivel de un vaso coronario.(2) Esta situación está dada por la presencia de factores de riesgo como hipertensión arterial, dislipidemia, sedentarismo, obesidad, entre otras circunstancias las cuales aceleraran el proceso de estrechez y taponamiento arterial, debutando una serie de episodios que concluirán en el Síndrome coronario agudo.(3) Finalmente esto se traducirá como un desequilibrio por una disminución del aporte coronario de oxígeno y el incremento de la demanda miocárdica de oxígeno. (5) (3)

1.1.4 Diagnostico

En base a la actualización de la Guía Europea y Americana del Síndrome coronario agudo, la recomendación 1A, es que todo paciente con sospecha de Síndrome coronario agudo sin elevación del segmento ST, el diagnóstico y estratificación del riesgo isquémico, debe ser primordial, combinando la historia clínica, sintomatología asociada, hallazgos físicos, Biomarcadores y la monitorización cardiaca mediante realización del Electrocardiograma con 12 derivaciones, teniendo especial importancia en las modificaciones del segmento ST.(2)(3)

1.1.4.1 Cuadro clínico

La descripción del cuadro clínico de parte del paciente o del familiar será; la presencia de dolor precordial, opresivo, de inicio brusco que puede o no estar relacionada al esfuerzo físico, se localiza generalmente retro esternal el cual suele ser irradiado al cuello, mandíbula y miembro superior izquierdo, se puede acompañar de síntomas neurovegetativos como nauseas, vomito, diaforesis, palidez generalizada, debilidad, entre otras.(6) Este cuadro clínico es de intensidad variable puede tener una duración de aproximadamente 20 minutos y se alivia tras la administración de tratamiento farmacológico. (1) Al examen físico regional el paciente se encuentra taquicardico, piel

pálida fría y diaforética. Es importante la auscultación cardiaca de un tercer o cuarto ruido agregado, además de estertores crepitantes a nivel de bases pulmonares, u otras manifestaciones clínicas de difusión ventricular.(2)

1.1.4.2 Factores de riesgo

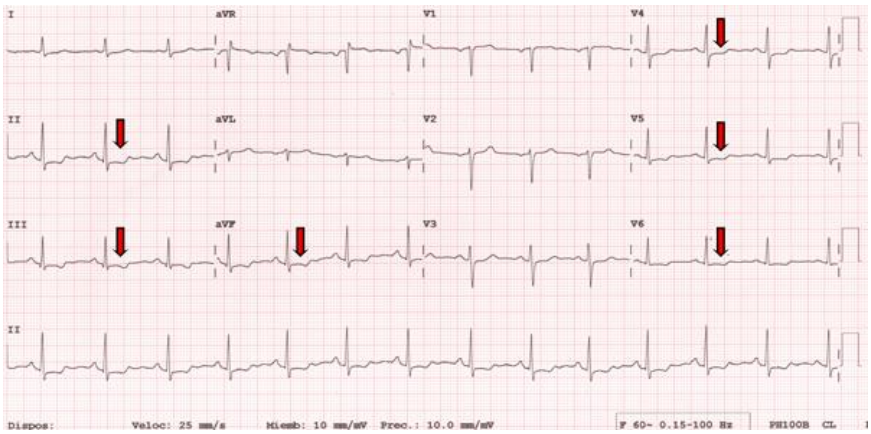
- Edad se observa mayor padecimiento en pacientes mayores de 65 años.
- Género: por lo general se observa en pacientes de sexo masculino.
- Hábitos tóxicos como es el consumo de alcohol, tabaco y estupefacientes.
- Antecedentes personales y familiares de cardiopatías, especialmente de infarto agudo de miocardio
- Antecedentes de revascularización
- Enfermedades concomitantes: hipertensión arterial, diabetes mellitus, síndrome metabólico e insuficiencia renal. (7)

1.1.4.3 Electrocardiograma

La realización e interpretación del Electrocardiograma con sus 12 derivaciones, debe ser realizado tan pronto como se recibe al paciente por el área de emergencia con signos y síntomas cardiológicos. (2)

Las singularidades que podremos encontrar en el electrocardiograma correspondería a un el descenso rectilíneo del segmento ST mayor o igual de 0.05mV, en dos o más derivaciones continuas, además de cambios en la onda T por presencia de isquemia cardiaca. (1)

Ilustración 1 Trazado electrocardiograma de SCA sin elevación del ST



Roffi M, Patrono C, Collet JP, Mueller C, Valgimigli M, Andreotti F, et al. 2015 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent st-segment elevation: Task force

1.1.4.4 Biomarcadores

Los Biomarcadores constituyen un valor fundamental dentro del diagnóstico y tratamiento de esta patología. Estos deben elevarse aproximadamente 10 veces superior a su valor normal para considerarlo un criterio factible para el síndrome coronario agudo sin elevación del segmento ST. (3)

CPK-MB: conocida como creatina quinasa mioglobina, se eleva en un lapso de 4-6 horas máximo 24 horas, desapareciéndose de 40-72 horas. (2)(3)

Troponina: es una proteína globular que se encuentra en el musculo esquelético, estriado y cardiaco. Siendo su valor normal 1-2 mg/dl. (2)(3)

Troponina T tipo II es la que se encuentra en el musculo cardiaco tiene gran sensibilidad, su valor normal es 14mg/L. Sus valores se normalizan al cabo de 7 días. (2) (1)

Mediante una revisión de un estudio retrospectivo de 1097 pacientes ingresados en una unidad hospitalaria se realizó un seguimiento debido a la presencia de valores elevados de Troponina en pacientes que no padecen síndrome coronario, de los cuales se realizó el biomarcador químico para Troponina T y la Troponina I correspondientes a proteínas cardiacas. (8) Los resultados obtenidos fueron que pese a que los pacientes que no padecían síndrome coronario agudo presentaban niveles elevados de troponinas 3 veces mayor a lo normal, los pacientes que si ingresaron por síndrome coronario agudo mostraron niveles de troponinas 1 veces mayor a su valor normal. (8)

Es importante la realización de controles periódicos de las enzimas cardiacas al momento del ingreso, después de 6 a 9 horas hasta que se decida el alta médica, dado que mientras más elevadas se encuentren los Biomarcadores mayor riesgo desencadenara el paciente. (1)

Se describe la presencia de otros Biomarcadores de severidad aplicables al paciente con Síndrome coronario agudo.(2)

Proteína C reactiva: cuando el paciente muestra troponinas negativas y se observa elevación del PCR (mayor a 10mg/L) se considera que este tendrá una alta mortalidad a largo plazo mayor a 6 meses y continuara durante 4 años. (1)(2)

Péptido natriuretico: es un marcador con alta sensibilidad y específico para detectar la disfunción ventricular. (1)

1.1.4.5 Ecocardiograma

El ecocardiograma transtoracico es un estudio secundario en los pacientes con síndrome coronario agudo sin elevación del segmento ST. (1) La realización de este examen no invasivo, se detectara el sitio de isquemia miocárdica, ya que puede mostrar una hipocinesia transitoria localizada o acinesia en segmentos de las paredes ventriculares, dependiendo del grado de afectación, la cual se normalizara al momento que se resuelva la isquemia mediante tratamiento farmacológico o quirúrgico. (7)

1.1.5. Evaluación del riesgo

La determinación y clasificación del riesgo del paciente, se ha simplificado mediante el uso de tablas con determinantes de riesgo, las cuales han sido desarrollas tras estudios científicos sistematizados que ayudara al profesional a un mejor manejo y tratamiento del paciente. (2)

No todos los pacientes con Síndrome coronario sin elevación del segmento ST, tienen el mismo riesgo de complicaciones durante la evolución (9)(3)

En esta patología los riesgos más importantes a valorar son;

Riesgo isquémico en las cuales se destaca GRACE y TIMI (10)

Riesgo hemorrágico se describe CRUSADE (11)

1.1.5.1 Escala GRACE

El termino GRACE o también conocido como Global Registry of Acute Coronary Events, determinara la estratificación del paciente en sus dos contextos; al momento de su ingreso y 6 meses posterior al su alta médica. (6)

En el año 2006 en Canadá se realizó un estudio retrospectivo, en el cual se determinaría la validez del Score Grace. De lo cual la cohorte fue de 1299 pacientes que fueron ingresados con diagnóstico de síndrome coronario agudo sin elevación del segmento ST. (12) En estos pacientes se realizó el estudio durante su ingreso y 6 meses después del alta médica indicando la proporción aceptada según GRACE para los pacientes con

revascularización, que mostraron una mejoría significativa en cuanto al pronóstico calculado. (12) Por lo cual se otorgó la validez al estudio GRACE ya que se observó una buena capacidad predictor de muerte del paciente dentro de los 6 meses. (12)

Tabla 1

ESCALA DE GRACE	
Parámetros	**Puntaje**
Edad	
<40	0
40-49	18
50-59	36
60-69	55
70-79	73
≥80	91
Presión arterial	
<80	63
80-99	58
100-119	47
120-139	37
140-159	26
160-199	11
≥200	0
Killip	
Clase I	0
Clase II	21
Clase III	43
Clase IV	64
Frecuencia cardiaca	
<70	0
70-89	7
90-109	13
110-149	23
150-199	36
≥200	46
Creatinina	
0-0,39	2
0,4-0,79	5
0,8-1,19	8
1,2-1,59	11
1,6-1,99	14
2-3,9	23
≥4	31
Otros factores de riesgo	
Paro cardiaco al ingreso	43
Biomarcadores elevados	15
Supra desnivel del ST	30

Bradshaw P, Ko DT, Newman AM, Donovan LR, Tu J V. Validity of the GRACE (Global Registry of Acute Coronary Events) acute coronary syndrome prediction model for six month post-discharge death in an independent data set. Heart. 2006;92(7):905–9.

Tabla 2

INTERPRETACION DE LA ESCALA GRACE		
Riesgo	**Puntaje**	**% mortalidad hospitalaria**
Bajo	≤ 108	<1
Intermedio	109-140	1-3
Alto	>140	>3
Riesgo	**Puntaje**	**%mortalidad 6 meses**
Bajo	≤88	<3
Intermedio	89-118	3-8
Alto	>118	>8

Bradshaw P, Ko DT, Newman AM, Donovan LR, Tu J V. Validity of the GRACE (Global Registry of Acute Coronary Events) acute coronary syndrome prediction model for six month post-discharge death in an independent data set. Heart. 2006;92(7):905–9.

De tal forma estratificó bien a los pacientes, y hubo una buena correspondencia entre la proporción de muertes observadas en la cohorte en estudio (EFFECT) relacionada a la validación de la escala GRACE. (12) (6)

1.1.5.2. Escala TIMI

La escala de riesgo TIMI que significa (Thrombolysis in Myocardial infarction), es un esquema predictivo de uso simple que clasifica el riesgo de muerte en un lapso de 30 días y eventos isquémicos de un paciente que ha presentado síndrome coronario agudo sin elevación del segmento ST y facilita un contexto para la toma de decisiones terapéuticas. (13)

En el año 2000, se realizo la revision de dos ensayos, fase 3, internacionales aleatorizados y doble ciego (TIMI 11B y ESSENCE) para la validacion y simplificacion de la escala TIMI . (13) El puntaje de riesgo TIMI describe siete variables pronosticas de las cuales destaca; pacientes con 65 años de edad o mas, presencia de al menos tres factores de riesgo coronario, estenosis coronaria previa, cambios electrocardiograficos del segmento ST, al menos dos sucesos anginales en 24 horas, administracion de aspirina siete dias previos, aumento de biomarcadores cardiacos. (13)

Tabla 3

VARIABLES INCLUIDAS EN LA ESCALA DE RIESGO TIMI	
Al menos 3 de los siguientes factores de riesgo:	1 punto
Historia familiar de coronariopatia	
Hipertension arterial	
Hipercolesterolemia	
Diabetes	
Fumador actual	
Edad mayor de 65 años	1 punto
Evidencia de enfermedad coronaria previa	1 punto
Uso de acido acetilsalicilico en los 7 dias previos	1 punto
Al menos 2 episodios anginosos en las ultimas 24h	1 punto
Alteraciones del segmento ST	1 punto
Elevacion de marcadores de daño miocardico	1 punto

Antman EM, Cohen M, Bernink PJLM, McCabe CH, Horacek T, Papuchis G, et al. The TIMI Risk Score for Unstable Angina/Non–ST Elevation MI. JAMA. 2000

El porcentaje de riesgo calculado a los 14 días de mortalidad dada por cualquier causa de infarto de miocardio nuevo o recurrente o isquemia recurrente grave va a requerir una revascularización urgente. (2)

Tabla 4

ESTRADIFICACION DE PUNTAJE	
Puntaje 0-1	4.7.% de riesgo
Puntaje 2	8.3 % de riesgo
Puntaje 3	13.2 % de riesgo
Puntaje 4	19.9% de riesgo
Puntaje 5	26.2 % de riesgo
Puntaje 6-7	40.9% de riesgo

Antman EM, Cohen M, Bernink PJLM, McCabe CH, Horacek T, Papuchis G, et al. The TIMI Risk Score for Unstable Angina/Non–ST Elevation MI. JAMA. 2000

Se realizó un estudio con una cohorte prospectiva de pacientes con diagnóstico de síndrome coronario agudo del año 2013 al 2014 de validación de los dos puntajes pronósticos de GRACE y TIMI. (10)

Los pacientes en estudio fueron 507 con una edad promedio de 65 años de los cuales mayor proporción fueron del sexo masculino el 43.8% a los cuales se les realizo los estudios de cabecera necesarios para su estatificación. (10)

Se clasificaron:

TIMI; en riesgo bajo 2,17% con revascularización percutánea el 36%, riesgo intermedio 77,91% revascularización percutánea 85% y 15% quirúrgico y de riesgo alto 19,92% revascularización percutánea 90% y 10% quirúrgico. (10)

GRACE; riesgo bajo 0,2% de estos el 0% se ravascularizo, de riesgo intermedio 65,29% fueron 84% revascularización percutánea y 16% quirúrgico y a los pacientes con riesgo alto 34,52% con revascularización percutánea 90% y 10% quirúrgico. (10)

Los resultados de este estudio confirman el valor predictivo de dos puntajes utilizados rutinariamente en la evaluación médica en el servicio de urgencias de los pacientes con síndrome coronario agudo sin elevación del segmento ST, con hallazgos a favor del puntaje GRACE al mes y a los 6 meses en comparación con el TIMI. (11) El score de riesgo GRACE es el que más ampliamente se ha sometido a estudios y seguimiento con el fin de comprobar su capacidad y efectividad predictiva. (6)

1.1.5.3. Escala CRUSADE

Los pacientes que han presentado un Sindrome coronario agudo a menudo son tratados de manera agresiva con terapias multiples de antitromboticos, los cuales se los considera medicamentos de primera eleccion de Evidencia 1A, el uso de estos medicamentos favore enormemente la recuperacion y mejoria del paciente, sin embargo su uso concomitante incrementa las complicaciones relacionadas al riesgo de sangrado.(2)(3) De esta manera se considero importante la estimacion y prediccion de hemorragias en estos pacientes para lo cual se desarrollo una herramienta util que evalua el riesgo de sangrado denominada CRUSADE. (14)

Tabla 5

PUNTAJE CRUSADE	
Predictor	**Puntaje**
Hematocrito de base	
<31	9
31-33,9	7
34-36,9	3
37-39,9	2
≥40	0
Depuración de creatinina (Cockcroft)	
≤15	39
16-30	35
31-60	28
61-90	17
91-120	7
>121	0
Genero	
Hombre	0
Mujer	8
Signos de insuficiencia cardiaca	
No	0
Si	6
Enfermedad vascular previa	
No	0
Si	6
Diabetes mellitus	
No	0
Si	6
Presión arterial sistólica (mmHg)	
≤90	10
91-100	8
101-120	5
121-180	1
181-200	3
≥201	5

Roffi M, Patrono C, Collet JP, Mueller C, Valgimigli M, Andreotti F, et al. 2015 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent st-segment elevation: Task force for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation of . Eur Heart J. 2016;37(3):267–315

Tabla 6

ESTRADIFICACION DE RIESGO DEL PUNTAJE CRUSADE	
Puntaje total (1-100)	**Riesgo sangrado %**
≤20 muy bajo	3,1
21-30 bajo	5,5
31-40 moderado	8,6
41-50 alto	11,9
>50 muy alto	19,5

Roffi M, Patrono C, Collet JP, Mueller C, Valgimigli M, Andreotti F, et al. 2015 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent st-segment elevation: Task force for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation of . Eur Heart J. 2016;37(3):267–315

A. Cordero, et al (2017) presenta un estudio observacional, prospectivo realizado a partir del año 2003 al 2013 en dos unidades hospitalarias donde se admitieron un total de 7060 pacientes con síntomas clínicos de dolor precordial de estos la cohorte final en estudio fueron 6997 en los cuales el objetivo fue la aplicación de la escala de GRACE y de CRUSADE en conjunto para evaluar la tasa de mortalidad y el riesgo de hemorragia tras la aplicación del tratamiento. (15) Los resultados obtenidos fueron que mientras más altos eran los valores de CRUSADE más riesgo de mortalidad presentaban según GRACE con un valor promedio de 140 de esto se demostró que el valor de CRUSADE estaba en aumento.(15) Durante el seguimiento de estos pacientes posterior a su alta médica, con su tratamiento recibido de betabloqueantes y la revascularización respectivamente, asociándose una baja mortalidad y las categorías de riesgo intermedio y alto de la escala GRACE y CRUSADE, las cuales asociaron un mayor riesgo de mortalidad. (15)

1.1.6 Tratamiento

1.1.6.1 Medidas de soporte

Es de vital importancia la atención primaria e inmediata del paciente cardiológico cuyo objetivo principal será la estabilización clínica con el fin de mejorar la sintomatología y reducir la morbimortalidad.(5) Se recomienda de igual manera el uso de oxigeno según necesidades ventilatorias consiguiendo una saturación de oxigeno superior a 90%(7)

1.1.6.2 Tratamiento isquémico

El uso de fármacos anti isquémicos, entre el más recomendado están los Betabloqueantes, los cuales reducirán el consumo miocárdico de oxígeno, mejorando la frecuencia cardiaca, presión arterial y la precarga, por ende mejoraremos la vasodilatación coronaria. (1) La evidencia científica determina como recomendación 1A, el uso a largo plazo del beta bloqueantes en pacientes con Insuficiencia cardiaca, fracción de eyección inferior a 40% o disfunción ventricular izquierda. (7)

Dentro de los fármacos anti anginosos se nombra los Nitratos, debido a que mejora la sintomatología de manera que reduce la precarga miocárdica y el volumen telediastolico del ventrículo izquierdo, lo cual se traduce como en una disminución del consumo miocárdico de oxígeno. (2)(7)En cuanto a las recomendaciones clase 1C se

indica el uso de Nitratos sublingual o intravenoso para potenciar su efecto, aliviando la angina.(2)

1.1.6.3 Tratamiento anti plaquetario

El manejo del tratamiento anti plaquetario es de rápida instauración, una vez establecido el diagnóstico del síndrome coronario agudo sin elevación dl segmento ST.(5) Su importancia radica en reducir las complicaciones isquémicas y la reincidencia de nuevos episodios aterotromboticos. (2)

El ácido acetilsalicílico es una recomendación clase 1A, en ausencia de contraindicaciones, se administra a todos los pacientes una dosis aproximada de 150-300mg diarios vía oral como dosis de 75-100mg como mantenimiento durante un régimen aproximado de dos años, independientemente del tratamiento adjunto. (16)(2)

Los inhibidores del receptor P2Y12, como es el Clopidogrel con una dosis de carga de 600mg y posteriormente 75mg diarios vía oral para manteamiento durante aproximadamente 9-12 meses, se ha demostrado la mejoría clínica de la combinación del Clopidogrel con el ácido acetilsalicílico. (3) El Clopidogrel una vez metabolizado solo un 15% queda disponible para ser un metabolito activo el cual inactivara los receptores P2Y12 plaquetarios de forma selectiva e irreversible, de esta manera inhibe la agregación plaquetaria inducida por el adenosinfosfato. (2)

El Prasugel se encuentra dentro del grupo de los anti plaquetarios por inhibir de forma irreversible al receptor P2Y12, fue aprobado por la FDA en el 2009 y actualmente se encuentra en uso, varios estudios sistematizados demostraron la mayor efectividad del Prasugel frente al Clopidogrel. La dosis de carga es de 60mg, mientras que la dosis de mantenimiento es de 10mg vía oral. (2)

En el estudio (TRITON-TIMI38) se realizó una comparación del Prasugel frente al Clopidogrel, obteniendo los siguientes resultados; está contraindicado el uso de Prasugel en pacientes con antecedentes de eventos cerebrovasculares y no presenta beneficio farmacológico en pacientes mayores de 75 años con peso corporal menor a 60kg. (17)

El estudio aleatorizado, controlado, doble ciego, fase 3 (TRILOGY ASC) de igual manera compara el Prasugel con el Clopidogrel en pacientes con síndrome coronario sin elevación del segmento ST con y sin intervencionismo se incluyó un total de 7243 pacientes menores de 75 años se realizó un seguimiento durante 30 meses.(9) De estos

pacientes un grupo se realizó angiografía y el otro no, recibiendo Clopidogrel y Prasugel respectivamente. Obteniéndose como resultado general que los pacientes que se les realizo angiografía y tomaron Prasugel presentaron menos muertes cardiovasculares, infartos de miocardio y eventos cerebrovascular que los pacientes que tomaron Clopidogrel. De tal manera demostrando mayor significancia para Prasugel. (9)

El Ticagrelor es el anti plaquetario, antagonista selectivo de los receptores de ADP actuando sobre el receptor P2Y12 inhibiendo la agregación y activación plaquetaria. (16)

Según la recomendación de las Guías clínicas de clase 1B, se recomienda el uso del Ticagrelor una dosis de carga es de 180mg, seguida de 90mg diarios vía oral, se incluye para todos los pacientes con riesgo isquémico de moderado a alto, es decir que Biomarcadores elevados, independiente de la estrategia de tratamiento inicial. (2)

El estudio PEGASUS-TIMI54, es un ensayo clínico aleatorizado, doble ciego, controlado con Placebo, con un total de 21162 pacientes sometidos a este estudio los cuales habían tenido síndrome coronario de 1 a 3 años.(18) Los pacientes fueron elegidos al azar para el estudio, un grupo de pacientes recibió Ticagrelor 90mg dos veces al día, el otro grupo 60mg de Ticagrelor dos veces al día y el otro grupo recibió placebo. Todos los pacientes sometidos al estudio debían tomar ácido acetilsalicílico de 75-150mg al día.(18) Los resultados obtenidos fueron que tomando en cuenta el riesgo beneficio se demostró en mayor parte que el uso del Ticagrelor en dosis de 90mg o 60mg dos veces al día añadida una dosis baja de ácido acetilsalicílico mejora significativamente el riesgo de muerte cardiovascular, infarto de miocardio o evento cerebrovascular, sin embargo aumentara el riesgo del sangrado dependiendo del TIMI del paciente. (18)

La guía clínica tanto Europea como Americana recomienda (Clase 1A) el uso de un inhibidor de la bomba de protones, en combinación con la anti agregación plaquetaria(2)(3)

1.1.6.4 Tratamiento antitrombotico

El uso de un anticoagulante intravenoso, conjuntamente con el antiplaquerario en los pacientes con síndrome coronario agudo, es una recomendación Clase 1 A de las guías de práctica clínica. (16) Señalando además la importancia del uso de un anticoagulante

más 2 anti plaquetarios entre estos el ácido acetilsalicílico y un inhibidor de los receptores P2Y12 como tratamiento de elección de primera línea. (2) (3)

La Bivalirudina se une directamente a la trombina, inhibiendo la conversión del fibrinógeno en fibrina inducida por la trombina. La Bivalirudina a dosis de 0,75 mg/ kg) intravenosa, en bolo, seguida de 1,75 mg /kg/h durante 4 horas, se considera una recomendación 1A.(2) (3)

El Fondaparinux es un inhibidor selectivo del factor Xa de la cascada de coagulación, antitrombotica.(16) Tras la revisión del estudio PENTUA en el 2005, la dosis fija de 2,5mg SC una vez al día, y su posterior confirmación con los estudios OASIS-5 y OASIS-6 respectivamente. De tal manera las guías coincidieron con la recomendación Clase 1B, de Fondaparinux 2mg por demostrar su eficacia y seguridad en cuanto a la anticoagulación.(2)(3)

De igual manera se sugiere el uso de Enoxaparina en dosis de 1mg/kg cada 12 horas durante 8 días, en pacientes mayores de 75 años se ajusta la dosis a 0.75mg/kg cada 12 horas. Siendo una recomendación clase 1B según las guías clínicas.(2) (3)

1.1.6.5 Tratamiento invasivo

La angiografía coronaria es considerado el Gold Estándar en cuanto a tratamiento se refiere en los pacientes con diagnóstico de Síndrome coronario agudo debido a la obstrucción del flujo sanguíneo. (19) La angioplastia es un procedimiento invasivo endovascular en el cual se utiliza una catéter con punta en forma de balón para abrir el vaso sanguíneo que se encuentra bloqueado. Posteriormente se coloca una malla metálica conocida como Stent la cual queda adherida a las paredes del vaso afecto.(16)

Un estudio prospectivo que determino el uso, momento y resultado de la angiografía coronaria, este seguimiento se lo realizo entre los años 2006 al 2014, en el que se incluyó 2299 pacientes de alto riesgo (GRACE >140) en la unidad cardiológica de Holanda. (19) El objetivo de este estudio era la importancia de las pautas de tratamiento de la realización de la angiografía coronaria dentro de las primeras 24 horas en pacientes con alto riesgo, el resultado mejoro en cuando a su pronóstico y calidad de vida, mostrando validez en cuanto a este estudio de intervencionismo. (19)(2)

Se realizó la revisión de un meta análisis de ensayos clínicos aleatorizados, incluyéndose 8 ensayos, la revisión consistió en la reducción de la mortalidad de los grupos que recibieron tratamiento invasivo inmediato, frente a los que el tratamiento invasivo fue retrasado.(20) Se demostró que la estrategia invasiva en los pacientes que

tenían más alto riesgo, es decir los que presentaron GRACE superior a 140 el tratamiento invasivo resulto mucho mejor de manera temprana, reduciendo la mortalidad. (20)
El manejo farmacológico y seguimiento a largo plazo, estableciendo la prevención secundaria con el fin de evitar nuevos eventos isquémicos. (16)

El uso de las estatinas está indicado en todos los pacientes independiente de los valores de colesterol, siendo una recomendación Clase 1B, se puede administrar atorvastatina 80mg vía oral diaria. (2) (3)

Tratamiento con los Inhibidores de la enzima convertidora de angiotensina, en pacientes con fracción de eyección ventrículo izquierdo inferior a 40%, hipertensión mal controlada, insuficiencia cardiaca y enfermedad renal crónica, la meta es conseguir presiones arteriales <140/90mgHg, esta es una recomendación Clase 1A. (2)(3)

Como ya se nombró anteriormente evidencia Clase 1A, el uso de betabloqueantes en pacientes con función sistólica ventricular izquierda reducida (FEVI ≤40%) (2)(3)

El uso de antialdosteronicos evidencia Clase 1A , para los pacientes que han sufrido de infarto agudo de miocardio que reciben IECA y Betabloqueantes con una fracción de eyección de ventrículo izquierdo ≤35%, con diabetes, insuficiencia cardiaca, enfermedad renal o hiperpotasemia.(2)(3)

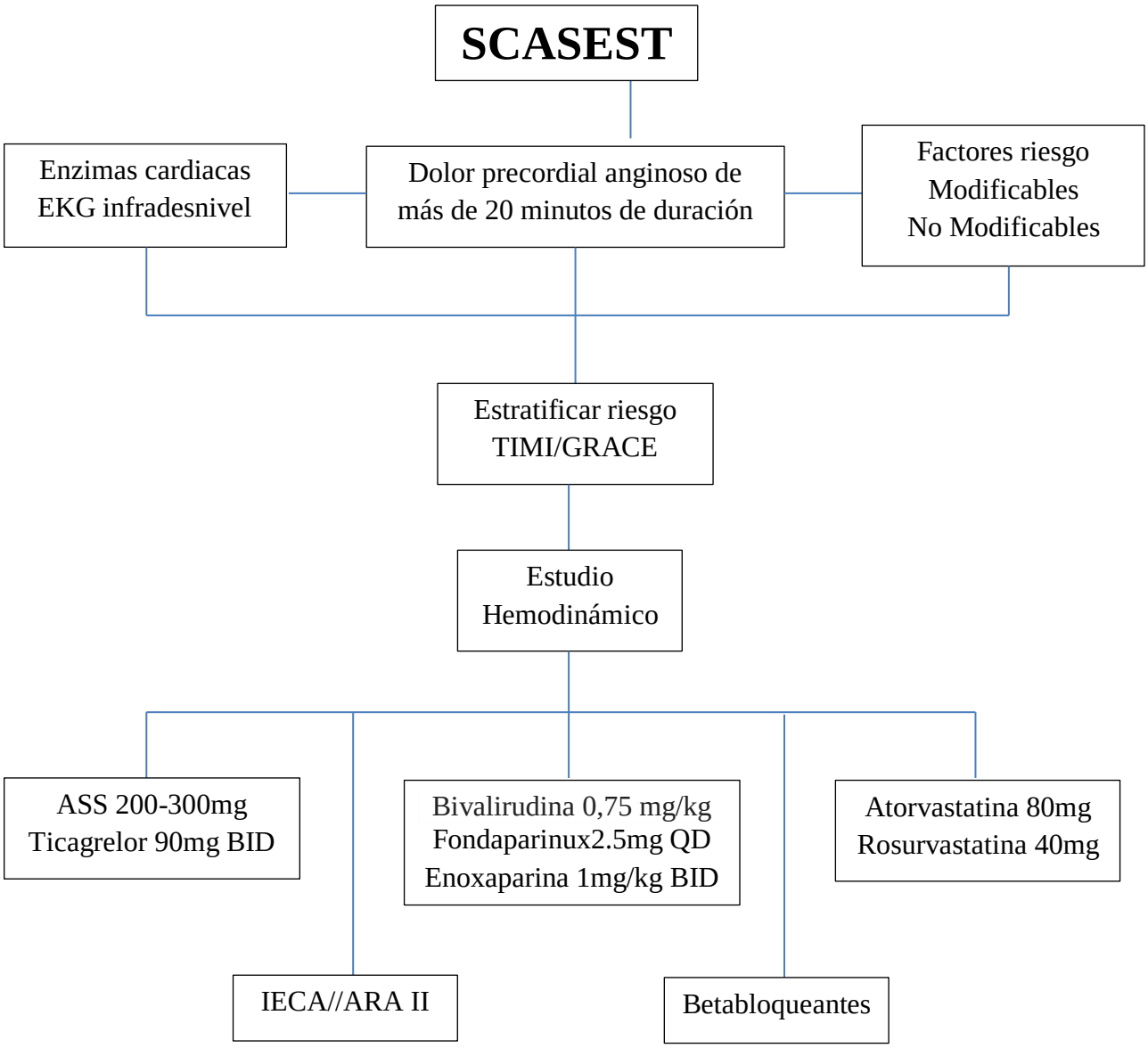
Además es importante la modificación del estilo de vida del paciente, siendo esta la piedra angular del tratamiento efectivo y su mejoría, ya que se ha demostrado tener un impacto mayor en cuanto a la supervivencia. Dentro de esto se describe los factores de riesgo modificables como el sedentarismo, la obesidad, los hábitos tóxicos, y una dieta adecuada.(1)

2. CONCLUSIONES

Todo paciente recibido en el área de emergencias con signos clínicos cardiológicos, es imprescindible el diagnóstico oportuno y la estratificación en cuanto al riesgo isquémico (TIMI-GRACE) y el riesgo hemorrágico (CRUSADE) para el manejo optimo , brindando el tratamiento farmacológico de la mejor evidencia que constituye el uso de oxigenoterapia, betabloqueantes, antiagregantes terapia dual, como el ácido acetilsalicílico y Ticagrelor, asociados a los inhibidores de la bomba de protones, anticoagulantes como Bivalirudina o Enoxaparina, estatinas, antialdosteronicos y siendo el Gold estándar en cuanto a intervencionismo.

Dentro del contexto de nuestra realidad, la situación económica y la infraestructura hospitalaria, la angioplastia coronaria no puede ser el tratamiento de primera elección en estos pacientes, debido a sus altos costos y falta de recursos, lo que sí es aplicable es la estratificación de riesgo mediantes las escalas ya nombradas y el tratamiento farmacológico. Sin embargo cabe recalcar que algunos de los medicamentos de primera elección, de la mejor recomendación no se encuentran dentro del ¨Cuadro Nacional de Medicamentos Básicos¨, por lo tanto no podríamos esperar reducir la morbimortalidad del paciente. Siendo esta las razones por lo cual se considera esta patología coronaria como la principal causa de muerte a nivel mundial, no por falta de conocimiento de parte del médico, sino por la falta de recursos y mejorías del sistema de salud.

Ilustración 2 ALGORITMO DE MANEJO DEL SINDROME CORONARIO AGUDO SIN ELEVACION DEL SEGMENTO ST



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4. ANEXOS

ESC European Society of Cardiology European Heart Journal (2018) 00, 1–33 doi:10.1093/eurheartj/ehy462

EXPERT CONSENSUS DOCUMENT

Fourth universal definition of myocardial infarction (2018)

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1. Thygesen K, Alpert JS, Jaffe AS, Chaitman BR, Bax JJ, Morrow DA, et al. Fourth Universal Definition of Myocardial Infarction (2018). Circulation [Internet]. 2018 (Citado 14 diciembre 2018);1–33. Available from: http://insights.ovid.com/crossref?an=00003017-900000000-95028

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ESC GUIDELINES

2015 ESC guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation

Task Force for the Management of Acute Coronary Syndromes in Patients Presenting without Persistent ST-Segment Elevation of the European Society of Cardiology (ESC)

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Councils: Council on Cardiovascular Nursing and Allied Professions (CCNAP), Council for Cardiology Practice (CCP), Council on Cardiovascular Primary Care (CCPC).

Working Groups: Working Group on Cardiovascular Pharmacotherapy, Working Group on Cardiovascular Surgery, Working Group on Coronary Pathophysiology and Microcirculation, Working Group on Thrombosis.

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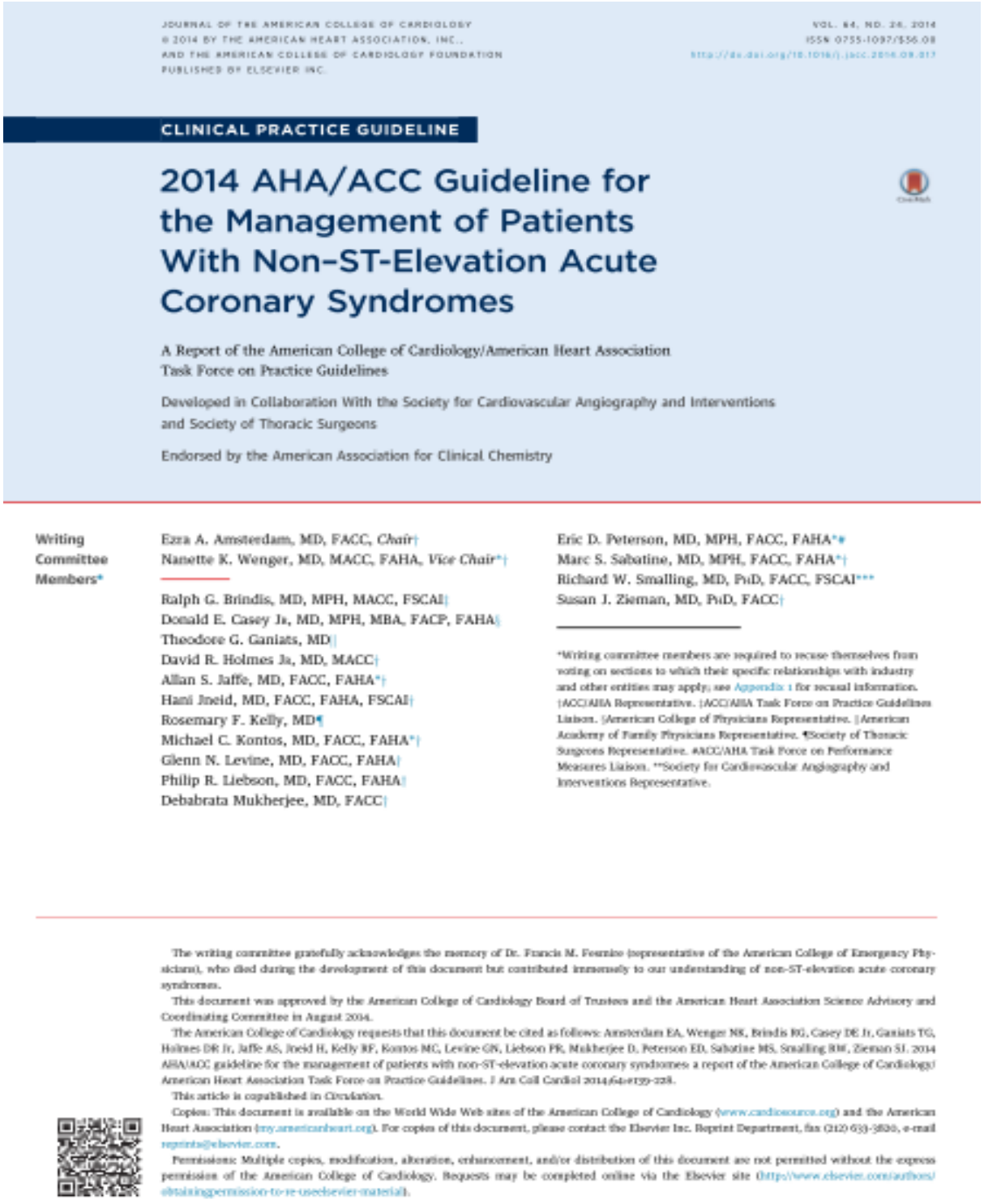

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CLINICAL PRACTICE GUIDELINE

2014 AHA/ACC Guideline for the Management of Patients With Non–ST-Elevation Acute Coronary Syndromes

A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines

Developed in Collaboration With the Society for Cardiovascular Angiography and Interventions and Society of Thoracic Surgeons

Endorsed by the American Association for Clinical Chemistry

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INVESTIGACIÓN CLÍNICA

Registro de síndromes coronarios agudos sin elevación del segmento ST en un centro hospitalario de tercer nivel de atención (estudio RESCATA-SEST)

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PALABRAS CLAVE
Angina inestable;
Infarto de miocardio sin elevación del ST;
Síndrome coronario agudo;
Síndrome coronario agudo sin elevación del ST;
Registros;
México

Resumen

Objetivo: Describir el perfil clinicoepidemiológico y el proceso de atención del síndrome coronario agudo sin elevación del segmento ST en un hospital de tercer nivel.

Método: Se analiza la información clínica, la estratificación de riesgo, la terapia de revascularización y los hábitos de prescripción al egreso de los casos con síndrome coronario agudo sin elevación del segmento ST atendidos en un año.

Resultados: Se incluyeron 283 pacientes con una edad media de 58 años; el 63%, masculino. La mayoría (88.6%) de los casos ocurrió entre los 50 y 59 años. La hipertensión arterial fue el factor de riesgo predominante. El 82.5% de los sujetos tuvo índice TIMI de riesgo bajo-intermedio. En el 37% de los pacientes hubo isquemia residual y en 80 (70%) se demostraron obstrucciones coronarias. Setenta y dos pacientes (90%) fueron revascularizados con stent, principalmente farmacológico (87.5%). Más del 90% de los casos recibió estatina y antiplaquetarios al egreso; otros medicamentos se indicaron en poco más del 50%.

Conclusiones: En la población estudiada, el síndrome coronario agudo sin elevación del ST predomina en hombres relativamente jóvenes e hipertensos. Estratificar el riesgo, buscar isquemia residual y revascularizar con stent farmacológico son prácticas comunes; el cumplimiento de las recomendaciones basadas en la evidencia es subóptimo.

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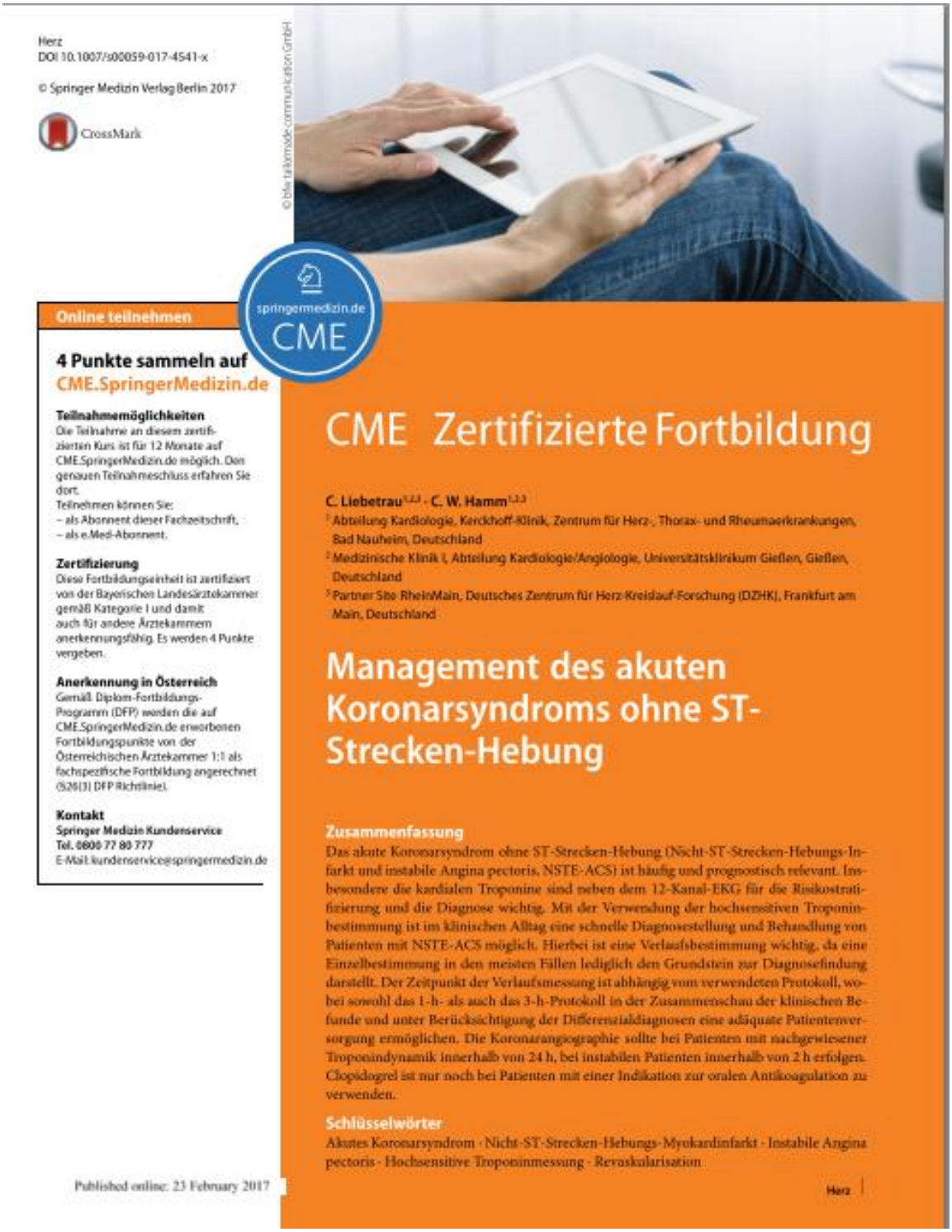

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Management des akuten Koronarsyndroms ohne ST-Strecken-Hebung

Zusammenfassung
Das akute Koronarsyndrom ohne ST-Strecken-Hebung (Nicht-ST-Strecken-Hebungs-Infarkt und instabile Angina pectoris, NSTE-ACS) ist häufig und prognostisch relevant. Insbesondere die kardialen Troponine sind neben dem 12-Kanal-EKG für die Risikostratifizierung und die Diagnose wichtig. Mit der Verwendung der hochsensitiven Troponinbestimmung ist im klinischen Alltag eine schnelle Diagnosestellung und Behandlung von Patienten mit NSTE-ACS möglich. Hierbei ist eine Verlaufsbestimmung wichtig, da eine Einzelbestimmung in den meisten Fällen lediglich den Grundstein zur Diagnosefindung darstellt. Der Zeitpunkt der Verlaufsmessung ist abhängig vom verwendeten Protokoll, wobei sowohl das 1-h- als auch das 3-h-Protokoll in der Zusammenschau der klinischen Befunde und unter Berücksichtigung der Differenzialdiagnosen eine adäquate Patientenversorgung ermöglichen. Die Koronarangiographie sollte bei Patienten mit nachgewiesener Troponindynamik innerhalb von 24 h, bei instabilen Patienten innerhalb von 2 h erfolgen. Clopidogrel ist nur noch bei Patienten mit einer Indikation zur oralen Antikoagulation zu verwenden.

Schlüsselwörter
Akutes Koronarsyndrom · Nicht-ST-Strecken-Hebungs-Myokardinfarkt · Instabile Angina pectoris · Hochsensitive Troponinmessung · Revaskularisation

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Frailty is associated with worse outcomes in non-ST-segment elevation acute coronary syndromes: Insights from the TaRgeted platelet Inhibition to cLarify the Optimal strateGy to medicallY manage Acute Coronary Syndromes (TRILOGY ACS) trial

Harvey D White[1], Cynthia M Westerhout[2], Karen P Alexander[3,4], Matthew T Roe[3,4], Kenneth J Winters[5], Derek D Cyr[3], Keith AA Fox[6], Dorairaj Prabhakaran[7], Judith S Hochman[8], Paul W Armstrong[2,9] and E Magnus Ohman[3,4] for the TRILOGY ACS investigators

Abstract

Aims: Little is known regarding consequences of frailty in patients with acute coronary syndrome (ACS). We assessed the associations of frailty and outcomes in ACS patients who were participating in a clinical trial.

Methods and results: The TaRgeted platelet Inhibition to cLarify the Optimal strateGy to medicallY manage Acute Coronary Syndromes (TRILOGY ACS) trial randomized 9326 patients planned for medical management to prasugrel or clopidogrel. The primary endpoint was a composite of cardiovascular death, myocardial infarction (MI), or stroke over a period of 30 months. A frailty score based upon the Fried score was self-reported at baseline in patients aged ≥65 years. Five frailty questions were recorded for 4996/5102 (97.9%) patients: 72.3% were classified as not-frail (0 items), 23.0% as pre-frail (1–2 items), and 4.7% as frail (≥3 items). Increasing frailty score was associated with older age, diabetes, and higher Global Registry of Acute Coronary Events (GRACE) scores. Frailty was associated with a higher unadjusted incidence of the primary endpoint (pre-frail vs not-frail: 29.2% vs 23.1%; hazard ratio [HR]: 1.39; 95% confidence interval [CI]: 1.19–1.61; $p<0.001$; frail vs not-frail: 39.7% vs 23.1%; HR: 1.76; 95% CI: 1.36–2.28; $p<0.001$), and all-cause mortality (pre-frail vs not-frail: 21.7% vs 15.0%; HR: 1.45; 95% CI: 1.22–1.73; $p<0.001$; frail vs not-frail: 30.2% vs 15.0%; HR: 1.98; 95% CI: 1.47–2.68; $p<0.001$). After adjustment for baseline characteristics and GRACE covariates, frailty remained independently associated with the primary endpoint: pre-frail vs not-frail, HR: 1.33; 95% CI: 1.15–1.54; $p<0.001$; frail vs not-frail, HR: 1.52; 95% CI: 1.18–1.98; $p=0.002$. There was no association of frailty with bleeding.

Conclusion: Frailty is associated with the composite of cardiovascular death, MI, or stroke. Frailty assessment contributes to risk prediction and adds to the GRACE score.

Keywords

Frailty, acute coronary syndrome, outcome assessment, clinical trial, elderly

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Fast assessment and management of chest pain without ST-elevation in the pre-hospital gateway: Rationale and design

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Abstract

Background: For chest pain patients without ST-segment elevation in the pre-hospital setting, current clinical guidelines merely offer in-hospital risk stratification and management, as opposed to chest pain patients with ST-segment elevation for whom there is a straightforward pre-hospital strategy for diagnosis, medication regimen and logistics. The FAMOUS TRIAGE study will assess the effects of introducing a pre-hospital triage system that reliably stratifies chest pain patients without ST-segment elevation into 1) patients at high risk for NSTEMI requiring a direct transfer to a PCI-hospital; 2) patients at intermediate risk for a major adverse cardiac event (MACE) who could be evaluated at the nearest non-PCI hospital; and 3) patients at low risk for MACE (benign non-cardiac chest pain) who could have further evaluation at home or in a primary care setting.

Methods: The FAMOUS TRIAGE study will be performed in three phases. In the first phase an appropriate pre-hospital risk stratification tool will be designed for chest pain patients without ST-segment elevation by means of a retrospective and a prospective study. The second phase of the project represents the external validation of the risk stratification models, and in the third and final phase an optimal risk stratification tool will be implemented into clinical practice. Clinical and economical endpoints before and after implementation of the pre-hospital risk stratification tool will be compared to assess clinical benefit and cost-effectiveness.

Conclusion: The FAMOUS TRIAGE project is a triple phase study that aims to optimize the pre-hospital management of chest pain patients without ST-segment elevation by providing tools for pre-hospital identification of NSTEMI or exclusion of acute coronary syndrome at home. TRIAL ID: NTR4205. Dutch Trial Register [http://www.trialregister.nl]: trial number 4205

Keywords

Acute coronary syndrome, acute myocardial infarction, chest pain, non ST-elevation acute coronary syndrome, non ST-elevation myocardial infarction, unstable angina, ACS, AMI, NSTEMI, nonSTEMI, UA, ambulance, paramedic, pre-hospital, triage, risk stratification, FAMOUS TRIAGE, modified HEART score, high-sensitive troponin

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Prevalence and significance of troponin elevations in patients without acute coronary disease☆,☆☆

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ABSTRACT

Background: Cardiac troponin T and I are important diagnostic and prognostic markers in patients with acute coronary syndrome (ACS). Troponin elevations in various non-ACS scenarios have been documented, but few studies have been conducted on the general hospitalized population, none compared the diagnostic performance of troponin I and T.

Methods and results: Patients aged >18 years (n = 1097), consecutively admitted to a district hospital, were included in the study. Blood samples were collected at admission and analysed with three different troponin assays. Serum was available in 92.2%, giving a study population of 1012 patients (mean age 61.6 years, 510 (50.4%) female).

ACS was diagnosed among 125 (12.4%) of the patients. Remaining patients were admitted with a broad spectrum of medical and surgical conditions. Of the total population, sc-cTnI was above the 99th percentile in 93 (9.2%), hs-cTnI was above the 99th percentile in 80 (7.9%) and hs-cTnT was above the 99th percentile in 400 (39.5%) of the patients ($p < 0.001$ for all differences). Hs-cTnT was stronger correlated with estimated glomerular filtration rate ($r[2] = 0.13$ vs $r[2] = 0.06$) and haemoglobin ($r[2] = 0.1$ vs $r2 = 0.02$) than with hs-cTnI, none were correlated with C-reactive protein ($r[2] = 0.04$ vs $r[2] = 0.02$).

The correlation between ln(hs-cTnT) and ln(hs-cTnI) was better in ACS patients than in non-ACS patients ($r[2] = 0.79$ vs $r[2] = 0.47$, $p < 0.001$).

Conclusion: Hs-cTnT was elevated above the 99th percentile in more than one third of the non-ACS patients, while hs-cTnI and sc-cTnI were elevated in approximately one tenth. The correlation between hs-cTnT and hs-cTnI concentrations was significantly stronger in ACS patients than in non-ACS patients.

1. Introduction

The cardiac troponin T (cTnT) and I (cTnI) are well-established markers of myocardial necrosis and their expression is considered to be specific for myocardial cells [1]. They therefore play a key role in the clinical diagnosis of, and risk stratification in, acute coronary syndrome (ACS) [2].

In recent years, studies have reported troponin elevations in a variety of non-ACS conditions. These include populations of patients with stable coronary artery disease (CAD), non-ischemic heart diseases, stroke, sepsis, chronic obstructive lung disease and renal failure, as well as in unselected intensive-care unit patients. In healthy people, excessive physical exercise may increase the troponin level [3–24].

Studies of a general population found elevations (above the 99th percentile) of high-sensitivity (hs) cTnT in 5.2%–7.4% of subjects aged 60–74, and elevations were correlated with increased mortality [25,26].

While the improved sensitivity of the hs-cTnT assays has been thoroughly described, this is not the case for the more recently developed

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☆☆ All work was performed at Nordsjællands University Hospital of Copenhagen, Nordsjælland, Dyrehavevej 29, 3400 Hillerød, Denmark.

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Spontaneous MI After Non–ST-Segment Elevation Acute Coronary Syndrome Managed Without Revascularization

The TRILOGY ACS Trial

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ABSTRACT

BACKGROUND Patients with acute coronary syndrome (ACS), especially those receiving medical management without revascularization, are at high risk for spontaneous myocardial infarction (MI), but its frequency and predictors are unknown.

OBJECTIVES This study sought to characterize spontaneous MI events in a randomized population during 30 months of follow-up and develop a prediction model for spontaneous MI to assign risk of spontaneous MI events in ACS populations.

METHODS We analyzed data from the randomized TRILOGY ACS (TaRgeted platelet Inhibition to cLarify the Optimal strateGy to medically manage Acute Coronary Syndromes) trial of aspirin plus prasugrel or clopidogrel following ACS. The trial included 9,326 patients with non-ST-segment elevation myocardial infarction (NSTEMI)/unstable angina (UA) who were managed medically without planned revascularization. Our study population included 9,294 patients. A multivariable Cox proportional hazards model was developed to determine predictors of time to first spontaneous MI event through 30 months. After model validation, we developed a calculator for model implementation.

RESULTS Among 9,294 patients, 695 spontaneous MI events occurred over a median of 17 months, representing 94% of adjudicated MI events (n = 737). The Kaplan-Meier event rate of spontaneous MI through 30 months was 10.7%. The strongest predictors of spontaneous MI were older age, NSTEMI versus UA as index event, diabetes mellitus, no pre-randomization angiography, and higher baseline creatinine values. The model exhibited good predictive capabilities (c-index = 0.732) and had good calibration, especially for patients with low-to-moderate risk of spontaneous MI.

CONCLUSIONS Spontaneous MI following a medically managed UA/NSTEMI event is common. Baseline characteristics can be used to predict subsequent risk of spontaneous MI in this population. These findings provide insight into the long-term natural history of medically managed UA/NSTEMI patients and could be used to optimize risk stratification and treatment of these patients. (A Comparison of Prasugrel and Clopidogrel in Acute Coronary Syndrome Subjects [TRILOGY ACS]; NCT00699998) (J Am Coll Cardiol 2016;67:1289–97) © 2016 by the American College of Cardiology Foundation.

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CARDIOLOGÍA DEL ADULTO – ARTÍCULO ORIGINAL

Validación y comparación de los puntajes TIMI y GRACE en pacientes con síndrome coronario agudo sin elevación del segmento ST

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PALABRAS CLAVE
Síndrome coronario agudo;
Validación;
Pronóstico

Resumen
Introducción: La validación y comparación de los modelos de predicción clínica es recomendable puesto que pueden tener diferente desempeño en las poblaciones de acuerdo con características étnicas, socio-demográficas, genéticas, culturales o idiosincráticas.
Metodología: Estudio de validación y comparación de dos escalas de pronóstico en una cohorte prospectiva de pacientes mayores de 18 años de edad con diagnóstico de síndrome coronario agudo sin elevación del segmento ST.
Resultados: Se incluyeron 507 pacientes en el análisis. El promedio de edad fue de 65 ± 11 años, el 54,4% tenía más de 65 años, el 55,6% era de sexo masculino, el 43,8% tenía al menos tres factores de riesgo coronario y el tipo de síndrome coronario fue angina inestable en un 52,3% e infarto de miocardio sin elevación del segmento ST en un 47,7%. La distribución de mortalidad hospitalaria (n = 21, 4,1%) por cualquier causa, contrasta entre los diversos grupos de riesgo, con diferencias significativas para ambos puntajes (TIMI p = 0,00001; GRACE p = 0,0016); al igual que para el GRACE extrahospitalario (p = 0,00001). La calibración de los modelos fue adecuada (Hosmer Lemeshow > 0,05). La discriminación del desenlace aislado de muerte fue buena para ambas escalas en el escenario intrahospitalario (AUC-ROC TIMI 0,75 vs. GRACE 0,79, p = 0,37), con diferencias significativas a 30 días (AUC-ROC TIMI 0,71 vs. GRACE 0,85, p = 0,0049) y a 6 meses (AUC-ROC TIMI 0,75 vs. GRACE 0,84, p = 0,0194) a favor de la escala GRACE.

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Does Simplicity Compromise Accuracy in ACS Risk Prediction? A Retrospective Analysis of the TIMI and GRACE Risk Scores

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Abstract

Background: The Thrombolysis in Myocardial Infarction (TIMI) risk scores for Unstable Angina/Non-ST–elevation myocardial infarction (UA/NSTEMI) and ST-elevation myocardial infarction (STEMI) and the Global Registry of Acute Coronary Events (GRACE) risk scores for in-hospital and 6-month mortality are established tools for assessing risk in Acute Coronary Syndrome (ACS) patients. The objective of our study was to compare the discriminative abilities of the TIMI and GRACE risk scores in a broad-spectrum, unselected ACS population and to assess the relative contributions of model simplicity and model composition to any observed differences between the two scoring systems.

Methodology/Principal Findings: ACS patients admitted to the University of Michigan between 1999 and 2005 were divided into UA/NSTEMI (n = 2753) and STEMI (n = 698) subpopulations. The predictive abilities of the TIMI and GRACE scores for in-hospital and 6-month mortality were assessed by calibration and discrimination. There were 137 in-hospital deaths (4%), and among the survivors, 234 (7.4%) died by 6 months post-discharge. In the UA/NSTEMI population, the GRACE risk scores demonstrated better discrimination than the TIMI UA/NSTEMI score for in-hospital (C = 0.85, 95% CI: 0.81–0.89, versus 0.54, 95% CI: 0.48–0.60; p<0.01) and 6-month (C = 0.79, 95% CI: 0.76–0.83, versus 0.56, 95% CI: 0.52–0.60; p<0.01) mortality. Among STEMI patients, the GRACE and TIMI STEMI scores demonstrated comparably excellent discrimination for in-hospital (C = 0.84, 95% CI: 0.78–0.90 versus 0.83, 95% CI: 0.78–0.89; p = 0.83) and 6-month (C = 0.72, 95% CI: 0.63–0.81, versus 0.71, 95% CI: 0.64–0.79; p = 0.79) mortality. An analysis of refitted multivariate models demonstrated a marked improvement in the discriminative power of the TIMI UA/NSTEMI model with the incorporation of heart failure and hemodynamic variables. Study limitations included unaccounted for confounders inherent to observational, single institution studies with moderate sample sizes.

Conclusions/Significance: The GRACE scores provided superior discrimination as compared with the TIMI UA/NSTEMI score in predicting in-hospital and 6-month mortality in UA/NSTEMI patients, although the GRACE and TIMI STEMI scores performed equally well in STEMI patients. The observed discriminative deficit of the TIMI UA/NSTEMI score likely results from the omission of key risk factors rather than from the relative simplicity of the scoring system.

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Introduction

Risk stratification is integral to the management of patients presenting with Acute Coronary Syndromes (ACS). Current AHA/ACC guidelines promote the use of the Thrombolysis in Myocardial Infarction (TIMI) and Global Registry of Acute Coronary Events (GRACE) risk scores to evaluate the in-hospital and post-discharge risk of ACS patients [1]. Both of these scoring systems have been shown to predict the response of ACS patients to various treatment modalities, and may therefore significantly influence therapeutic decision-making [2,3,4]. The TIMI risk scores for Unstable Angina/Non ST-Elevation Myocardial Infarction (UA/NSTEMI) and for ST-Elevation Myocardial Infarction (STEMI) patients are simple, integer-based scores derived from selected clinical-trial cohorts [2,5]. Though slightly more complex, the GRACE risk scores for in-hospital and 6-

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CARDIOVASCULAR MEDICINE

Validity of the GRACE (Global Registry of Acute Coronary Events) acute coronary syndrome prediction model for six month post-discharge death in an independent data set

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Objective: To determine the validity of the GRACE (Global Registry of Acute Coronary Events) prediction model for death six months after discharge in all forms of acute coronary syndrome in an independent dataset of a community based cohort of patients with acute myocardial infarction (AMI).
Design: Independent validation study based on clinical data collected retrospectively for a clinical trial in a community based population and record linkage to administrative databases.
Setting: Study conducted among patients from the EFFECT (enhanced feedback for effective cardiac treatment) study from Ontario, Canada.
Patients: Randomly selected men and women hospitalised for AMI between 1999 and 2001.
Main outcome measure: Discriminatory capacity and calibration of the GRACE prediction model for death within six months of hospital discharge in the contemporaneous EFFECT AMI study population.
Results: Post-discharge crude mortality at six months for the EFFECT study patients with AMI was 7.0%. The discriminatory capacity of the GRACE model was good overall (C statistic 0.80) and for patients with ST segment elevation AMI (STEMI) (0.81) and non-STEMI (0.78). Observed and predicted deaths corresponded well in each stratum of risk at six months, although the risk was underestimated by up to 30% in the higher range of scores among patients with non-STEMI.
Conclusions: In an independent validation the GRACE risk model had good discriminatory capacity for predicting post-discharge death at six months and was generally well calibrated, suggesting that it is suitable for clinical use in general populations.

Patients who have been hospitalised for acute myocardial infarction (AMI) remain at increased risk for cardiovascular death in the year after discharge. In a cohort of 1299 patients Proom *et al*[1] found the risk for ischaemic events, including death, to be greatest in the first few weeks after AMI, declining rapidly up to 10 weeks and remaining in a steady state thereafter. Similarly, the period for increased risk for death among patients after a percutaneous catheter based intervention (PCI) complicated by a rise in cardiac enzymes is up to four months.[2] Risk scores can assist in identifying patients at increased risk for death within six months of discharge, for both patients with ST segment elevation AMI (STEMI) and patients with non-STEMI.[3]

The GRACE (Global Registry of Acute Coronary Events) study collected information from patients admitted with an acute coronary syndrome (ACS) to 94 hospitals in 14 countries in North and South America, Europe and the United Kingdom, and Australia and New Zealand. Overall 32% of patients were classified as having STEMI, 27% non-STEMI and 41% unstable angina.[4] The data were collected between 1999 and 2002. The GRACE model for calculating the risk for all cause mortality at six months after discharge from hospital among patients across the spectrum of ACS was developed and validated in cohorts from the GRACE registry.[3] The GRACE ACS risk model has also been published as an online risk calculator and in downloadable versions for hand-held devices (http://www.outcomes-umassmed.org/grace/acs_risk.cfm). The risk model, based on information available during the hospital stay, has not yet been tested in an independent AMI population.

METHODS

The EFFECT (enhanced feedback for effective cardiac treatment) study has been described previously.[5] Briefly, EFFECT AMI is a cluster, randomised trial to determine whether early versus late feedback of hospital adherence to evidence based performance indicators improves the quality of AMI care.

Study population

For phase I of the EFFECT study all patients admitted to hospitals in the province of Ontario, Canada, during the fiscal years 1999/2000 and 2000/01 with a most responsible diagnosis of AMI (*International classification of diseases*, ninth revision, code 410), and who had not been admitted for AMI in the year prior, were identified from the Canadian Institute for Health Information's Discharge Abstract Database. From this population a target sample of 125 patients from each site was randomly selected for each acute care hospital in the province that treated a minimum of 30 AMI cases per annum. Of 104 eligible acute care hospitals in Ontario, 103 (99%) from 85 corporations participated in the EFFECT study, making this a truly population based study. Early and late feedback groups were randomly assigned within hospital type. Hospitals were classified as small (fewer than 50 beds), community or teaching, as designated by the Ontario Joint

Abbreviations: ACS, acute coronary syndrome; AMI, acute myocardial infarction; EFFECT, enhanced feedback for effective cardiac treatment; GRACE, Global Registry of Acute Coronary Events; PCI, percutaneous catheter based intervention; STEMI, ST segment elevation acute myocardial infarction

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The TIMI Risk Score for Unstable Angina/Non–ST Elevation MI

A Method for Prognostication and Therapeutic Decision Making

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Context Patients with unstable angina/non–ST-segment elevation myocardial infarction (MI) (UA/NSTEMI) present with a wide spectrum of risk for death and cardiac ischemic events.

Objective To develop a simple risk score that has broad applicability, is easily calculated at patient presentation, does not require a computer, and identifies patients with different responses to treatments for UA/NSTEMI.

Design, Setting, and Patients Two phase 3, international, randomized, double-blind trials (the Thrombolysis in Myocardial Infarction [TIMI] 11B trial [August 1996–March 1998] and the Efficacy and Safety of Subcutaneous Enoxaparin in Unstable Angina and Non-Q-Wave MI trial [ESSENCE; October 1994–May 1996]). A total of 1957 patients with UA/NSTEMI were assigned to receive unfractionated heparin (test cohort) and 1953 to receive enoxaparin in TIMI 11B; 1564 and 1607 were assigned respectively in ESSENCE. The 3 validation cohorts were the unfractionated heparin group from ESSENCE and both enoxaparin groups.

Main Outcome Measures The TIMI risk score was derived in the test cohort by selection of independent prognostic variables using multivariate logistic regression, assignment of value of 1 when a factor was present and 0 when it was absent, and summing the number of factors present to categorize patients into risk strata. Relative differences in response to therapeutic interventions were determined by comparing the slopes of the rates of events with increasing score in treatment groups and by testing for an interaction between risk score and treatment. Outcomes were TIMI risk score for developing at least 1 component of the primary end point (all-cause mortality, new or recurrent MI, or severe recurrent ischemia requiring urgent revascularization) through 14 days after randomization.

Results The 7 TIMI risk score predictor variables were age 65 years or older, at least 3 risk factors for coronary artery disease, prior coronary stenosis of 50% or more, ST-segment deviation on electrocardiogram at presentation, at least 2 anginal events in prior 24 hours, use of aspirin in prior 7 days, and elevated serum cardiac markers. Event rates increased significantly as the TIMI risk score increased in the test cohort in TIMI 11B: 4.7% for a score of 0/1; 8.3% for 2; 13.2% for 3; 19.9% for 4; 26.2% for 5; and 40.9% for 6/7 ($P<.001$ by χ^2 for trend). The pattern of increasing event rates with increasing TIMI risk score was confirmed in all 3 validation groups ($P<.001$). The slope of the increase in event rates with increasing numbers of risk factors was significantly lower in the enoxaparin groups in both TIMI 11B ($P=.01$) and ESSENCE ($P=.03$) and there was a significant interaction between TIMI risk score and treatment ($P=.02$).

Conclusions In patients with UA/NSTEMI, the TIMI risk score is a simple prognostication scheme that categorizes a patient's risk of death and ischemic events and provides a basis for therapeutic decision making.

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PATIENTS PRESENTING WITH AN acute coronary syndrome without ST-segment elevation are diagnosed as having unstable angina/non–ST elevation myocardial infarction (MI) (UA/NSTEMI). Given the heterogeneous nature of UA/NSTEMI, such patients have a wide spectrum of risk for death and cardiac ischemic events.[1-5] Many attempts to estimate a gradient of risk among patients with UA/NSTEMI focus on a single variable, such as presence or absence of electrocardiographic (ECG) changes[6-9] or elevated serum cardiac markers.[10-13]

Prognostication schemes have been developed that categorize patients qualitatively into high, intermediate, or low risk, but they do not provide a quantitative statement about finer gradations of risk that exist clinically.[3] Although univariate analyses are informative as an initial assessment of the importance of a potential prognos-

See also p 876 and Patient Page.

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Original Article

CRUSADE bleeding score as a predictor of bleeding events in patients with acute coronary syndrome in Zagazig University Hospital

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ABSTRACT

Aim: To examine the value of CRUSADE bleeding score in predicting bleeding events in our local patients with acute coronary syndrome (ACS) in Zagazig University Hospitals.
Methods: Our study included 240 patients with ACS. They underwent history and clinical examination; 12-lead electrocardiography; echocardiography; troponin I, hematocrit value; estimated glomerular filtration rate (eGFR); application of CRUSADE score; and follow-up of the hospital stay and documentations of events. Patients were classified into two groups: Group I: patients with major bleeding, and Group II: patients without major bleeding.
Results: Patients with major bleeding were significantly older, with more diabetic and hypertensive patients, more prior vascular disease, heart failure, and less patients with unstable angina, higher heart rate and systolic blood, lower eGFR, and higher CRUSADE risk score.

CRUSADE bleeding score was the strongest predictor of major bleeding. Sensitivity of CRUSADE score ≥33 in prediction of major bleeding in the whole study group was 80%, specificity was 73.4%, positive predictive value was 26.9%, negative predictive value was 96.9%, overall accuracy was 74.1%. Sensitivity of CRUSADE score ≥38.5 in prediction of major bleeding in the STEMI patients was 70%, specificity was 84.8%, positive predictive value was 50%, negative predictive value was 92.9%, and overall accuracy was 82.1%.
Conclusion: CRUSADE score is a good predictor for major bleeding in Egyptian patients with ACS. It is applicable in UA/NSTEMI as well as in STEMI patients and in women as well as in men.

1. Introduction

Coronary artery disease (CAD) is one of the most important leading causes of death in the whole world.[1] Among the different clinical presentations of CAD, acute coronary syndrome (ACS) is the most important and life threatening condition.[2]

Different pathogeneses may share in the development of ACS. However, thrombosis is one of the most important blood

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Additive value of the CRUSADE score to the GRACE score for mortality risk prediction in patients with acute coronary syndromes

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ABSTRACT

Introduction: Acute coronary syndrome (ACS) treatments increase bleeding complications that also impair prognosis. Bleeding risk scores reclassification of actual mortality risk estimated by the GRACE score might improve overall estimation.
Methods: Observational and prospective study of all ACS patients admitted in two hospitals. Mortality risk was assessed by the GRACE score and bleeding risk by the CRUSADE score. We analyzed the net reclassification improvement (NRI) of adding the CRUSADE score to the GRACE score.
Results: We included 6997 patients, mean age 67.4 (12.9), 38.0% ST-elevation ACS, mean GRACE score 145.2 (39.9). The percentage of patients with CRUSADE score >20 or >50 increased as the GRACE score was higher. Hospital mortality was 5.3% and the addition of the CRUSADE score reclassified a relevant percentage of patients with GRACE score >109; NRI was 3.80% (1.10–6.10). During follow-up, (median 53.0 months) mortality rate was 22.6% and patients with CRUSADE score >50 had significantly higher mortality rates in all GRACE score categories; NRI was high (46.6%, 95% CI 41.0–53.1). The multivariate analysis outlined the independent predictive value of CRUSADE score >20 or >50 as well as GRACE scores 109–139 and >140.
Conclusions: The addition of the CRUSADE score to the GRACE score improved mortality risk estimation. A CRUSADE score >50 identified patients with higher post-discharge mortality and higher hospital mortality if GRACE score was >109. The CRUSADE score improved hospital and long-term mortality prediction in patients with GRACE score >140. Individual mortality risk estimation should integrate the CRUSADE and GRACE scores.

1. Introduction

Acute coronary syndromes (ACS) are heterogeneous processes trigged by intracoronary thrombosis that lead to myocardial ischemia [1]. Individual estimation of mortality risk has been clearly established for individual classification of hospital [2] and mid-term [3,4] prognosis. Among all the scales, the GRACE score has been widely accepted and endorsed by clinical guidelines [5]. Antiplatelet treatment and revascularization are the cornerstone of ACS treatment although they also increase the risk of bleeding complications [6]. The role of bleeding events has gained increased interest since they are also independent predictors of poorer outcomes [6].

Several features have been identified as independent predictors of bleeding, as age, previous bleeding, use dual antiplatelet or renal dysfunction, and most of them are also involved in ischemic risk [2,7–9]. The balance between mortality and bleeding risk can be determinant in many clinical decision-making such as revascularization [10,11], antiplatelet regimens and duration [12,13] or drug-eluting stents (DES) use [14]. Nevertheless, there is scarce evidence or recommendations regarding the integration of bleeding risk scales on daily clinical practice and patients' management [15–17].The aim of our study was to assess the role of CRUSADE bleeding score on reclassification for long-term mortality assessed by the GRACE score in a large cohort of ACS patients.

2. Methods

We designed a retrospective study of all consecutive patients admitted for ACS in two different centers. ACS was defined by presence of typical clinical symptoms of chest pain and electrocardiographic changes indicative of myocardial ischemia/lesion and/or elevation of serum markers of myocardial damage [5,13]. A total of 7060 patients were admitted for ACS between November 2003 and March 2013 and 63 were excluding for lacking of any variable need to assess the GRACE and CRUSADE risk scores; therefore,

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An update on management of the patient presenting with non-ST-elevation acute coronary syndromes

Antony G. Kaliyadan, Michael P. Savage, Nicholas Ruggiero II & David L. Fischman

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Clinical outcomes for prasugrel versus clopidogrel in patients with unstable angina or non-ST-elevation myocardial infarction: an analysis from the TRITON-TIMI 38 trial

Stefano De Servi[1], Jochen Goedicke[2], Andreas Schirmer[3] and Petr Widimsky[4]

Abstract

Aims: In the TRial to assess Improvement in Therapeutic Outcomes by optimizing platelet inhibitioN with prasugrel Thrombolysis In Myocardial Infarction 38 (TRITON-TIMI 38), prasugrel reduced the primary ischaemic endpoint as compared with clopidogrel in acute coronary syndrome (ACS) patients planned to undergo percutaneous coronary interventions, but increased the risk of bleeding. The present analysis shows the efficacy and safety data for the 10,074 non-ST segment elevation (NSTE)-ACS patients included in that trial.

Methods and results: The primary endpoint was significantly reduced by prasugrel in the overall NSTE-ACS population (hazard ratio (HR) 0.82, 95% confidence interval (CI) 0.73–0.93, p=0.002) as well as in unstable angina (UA) and in non-ST elevation myocardial infarction (NSTEMI) patient subgroups (interaction *p* value=0.39). Although non-coronary artery bypass graft (CABG) TIMI major bleeding was increased with prasugrel as compared with clopidogrel (HR 1.40, 95% CI 1.05–1.88, *p*=0.02), there was a net clinical benefit in patients assigned to prasugrel (HR 0.89, 95% CI 0.80–1.00, *p*=0.043), which was consistent for UA and NSTEMI subgroups (interaction p value=0.84 and 0.72). In patients who met the criteria for prasugrel use recommended by the European Medicines Agency, thus excluding from the analysis patients with prior transient ischemic attack (TIA)/stroke, with weight <60 kg or age ≥75 years, and censoring follow-up at 365 days, (European Union (EU)-label cohort) prasugrel showed superiority over clopidogrel with regard to the primary endpoint (HR 0.73, 95% CI 0.63–0.85, p<0.0001) for the entire NSTE-ACS population, as well as for UA patients and NSTEMI patients without significant differences in non-CABG TIMI major bleeding.

Conclusion: Prasugrel, as compared with clopidogrel, significantly reduced the primary endpoint of the TRITON-TIMI 38 trial in NSTE-ACS patients, as well as in the UA and NSTEMI groups. A significant reduction in the primary endpoint without increased bleeding was observed in the EU-label cohort.

Keywords

Acute coronary syndrome, percutaneous coronary intervention, prasugrel, clopidogrel

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Introduction

The novel $P2Y_{12}$ inhibitors, prasugrel and ticagrelor, which have been proven to be superior to clopidogrel in reducing thrombotic cardiovascular (CV) events in the respective TRial to assess Improvement in Therapeutic outcomes by Optimizing platelet inhibitioN with prasugrel Thrombolysis In Myocardial Infarction 38 (TRITON-TIMI 38) and

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Long-Term Use of Ticagrelor in Patients with Prior Myocardial Infarction

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ABSTRACT

BACKGROUND

The potential benefit of dual antiplatelet therapy beyond 1 year after a myocardial infarction has not been established. We investigated the efficacy and safety of ticagrelor, a $P2Y_{12}$ receptor antagonist with established efficacy after an acute coronary syndrome, in this context.

METHODS

We randomly assigned, in a double-blind 1:1:1 fashion, 21,162 patients who had had a myocardial infarction 1 to 3 years earlier to ticagrelor at a dose of 90 mg twice daily, ticagrelor at a dose of 60 mg twice daily, or placebo. All the patients were to receive low-dose aspirin and were followed for a median of 33 months. The primary efficacy end point was the composite of cardiovascular death, myocardial infarction, or stroke. The primary safety end point was Thrombolysis in Myocardial Infarction (TIMI) major bleeding.

RESULTS

The two ticagrelor doses each reduced, as compared with placebo, the rate of the primary efficacy end point, with Kaplan–Meier rates at 3 years of 7.85% in the group that received 90 mg of ticagrelor twice daily, 7.77% in the group that received 60 mg of ticagrelor twice daily, and 9.04% in the placebo group (hazard ratio for 90 mg of ticagrelor vs. placebo, 0.85; 95% confidence interval [CI], 0.75 to 0.96; P=0.008; hazard ratio for 60 mg of ticagrelor vs. placebo, 0.84; 95% CI, 0.74 to 0.95; P=0.004). Rates of TIMI major bleeding were higher with ticagrelor (2.60% with 90 mg and 2.30% with 60 mg) than with placebo (1.06%) (P<0.001 for each dose vs. placebo); the rates of intracranial hemorrhage or fatal bleeding in the three groups were 0.63%, 0.71%, and 0.60%, respectively.

CONCLUSIONS

In patients with a myocardial infarction more than 1 year previously, treatment with ticagrelor significantly reduced the risk of cardiovascular death, myocardial infarction, or stroke and increased the risk of major bleeding. (Funded by AstraZeneca; PEGASUS-TIMI 54 ClinicalTrials.gov number, NCT01225562.)

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Original Article

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Use, timing and outcome of coronary angiography in patients with high-risk non-ST-segment elevation acute coronary syndrome in daily clinical practice: insights from a 'real world' prospective registry

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Abstract

Background An early invasive strategy (EIS) is recommended in high-risk patients with non-ST-elevation acute coronary syndrome (NSTE-ACS), defined as coronary angiography (CAG), within 24 h of admission. The aim of the present study is to investigate guideline adherence, patient characteristics associated with timing of the intervention and clinical outcome.

Methods In a prospective registry, the use and timing of CAG and the characteristics and clinical outcome associated with timing were evaluated in high-risk ACS patients. The outcome of early versus delayed invasive strategy (DIS) was compared.

Results Between 2006 and 2014, 2,299 high-risk NSTE-ACS patients were included. The use of CAG increased from 77% in 2006 to 90% in 2014 (p trend <0.001) together with a decrease of median time to CAG from 23.3 to 14.5 h (p trend <0.001) and an increase of patients undergoing EIS from 50 to 60% (p trend = 0.002). Patient factors independently related to DIS were higher GRACE risk score, higher age and the presence of comorbidities. No difference was found in incidence of mortality, reinfarction or bleeding at 30-day follow-up. All-cause mortality at 1-year follow-up was 4.1% vs 7.0% in EIS and DIS respectively (hazard ratio 1.67, 95% confidence interval 1.12–2.49) but was comparable after adjustment for confounding factors.

Conclusion The percentage of high-risk NSTE-ACS patients undergoing CAG and EIS has increased in the last decade. In contrast to the guidelines, patients with a higher risk profile are less likely to undergo EIS. However, no difference in outcome after 30 days and 1 year was found after multivariate adjustment for this higher risk.

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What's new?

- For high-risk patients with non-ST-elevation acute coronary syndrome, guidelines recommend early invasive treatment (coronary angiography within 24 h of admission), but only 60% of patients are treated this way in clinical practice.
- In contrast to the guidelines, patients with a higher risk profile are less likely to undergo early invasive treatment.
- No difference in outcome was found between early and late invasive treatment at 30 days and 1 year following multivariate adjustment for risk factors.

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Optimal timing of an invasive strategy in patients with non-ST-elevation acute coronary syndrome: a meta-analysis of randomised trials

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Summary

Background A routine invasive strategy is recommended for patients with non-ST-elevation acute coronary syndromes (NSTE-ACS). However, optimal timing of invasive strategy is less clearly defined. Individual clinical trials were underpowered to detect a mortality benefit; we therefore did a meta-analysis to assess the effect of timing on mortality.

Methods We identified randomised controlled trials comparing an early versus a delayed invasive strategy in patients presenting with NSTE-ACS by searching MEDLINE, Cochrane Central Register of Controlled Trials, and Embase. We included trials that reported all-cause mortality at least 30 days after in-hospital randomisation and for which the trial investigators agreed to collaborate (ie, providing individual patient data or standardised tabulated data). We pooled hazard ratios (HRs) using random-effects models. This meta-analysis is registered at PROSPERO (CRD42015018988).

Findings We included eight trials (n=5324 patients) with a median follow-up of 180 days (IQR 180–360). Overall, there was no significant mortality reduction in the early invasive group compared with the delayed invasive group HR 0·81, 95% CI 0·64–1·03; p=0·0879). In pre-specified analyses of high-risk patients, we found lower mortality with an early invasive strategy in patients with elevated cardiac biomarkers at baseline (HR 0·761, 95% CI 0·581–0·996), diabetes (0·67, 0·45–0·99), a GRACE risk score more than 140 (0·70, 0·52–0·95), and aged 75 years older (0·65, 0·46–0·93), although tests for interaction were inconclusive.

Interpretation An early invasive strategy does not reduce mortality compared with a delayed invasive strategy in all patients with NSTE-ACS. However, an early invasive strategy might reduce mortality in high-risk patients.

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Introduction

Guidelines for the management of patients with non-ST-elevation acute coronary syndromes (NSTE-ACS) recommend an invasive strategy in moderate to high-risk patients.[1,2] Recommendations for the timing of intervention in these patients depend on patient's baseline risk. Immediate coronary angiography within 2 h of presentation is recommended for all patients with a very high risk of in-hospital mortality (ie, those with haemodynamic instability, life-threatening arrhythmia, or recurrent or refractory angina); the recommendation is based on expert opinion without any evidence from clinical trials. Coronary angiography within 24 h is advised for patients not meeting these criteria but presenting with elevated troponin or ischaemic ST-wave or T-wave changes as well as patients with a Global Registry of Acute Coronary Events (GRACE) risk score of more than 140 points. The recommendation is primarily based on a pre-specified subgroup analysis of the TIMACS trial,[3] in which the early invasive strategy was superior to the delayed invasive strategy with regard to the composite endpoint of death, myocardial infarction, or stroke at 6 months in the highest GRACE risk score tertile. However, the effect of an early invasive strategy on individual clinical endpoints such as mortality or non-fatal myocardial infarction is unknown; individual trials were underpowered to detect an effect on these outcomes.

Moreover, previous meta-analyses pooling published data did not detect a difference on these outcomes. Only recurrent or refractory ischaemia and length of hospital stay have been shown to be improved by an early invasive strategy compared with a delayed invasive strategy.[4–6] Because of inconsistent trial reporting, no subgroup analyses of high-risk patients were possible in these meta-analyses.

To overcome shortcomings of conventional meta-analyses, we did a collaborative meta-analysis of randomised controlled trials investigating optimal timing of coronary angiography in patients with NSTE-ACS, based on individual patient or standardised tabulated data not previously published. We analysed all-cause mortality overall and in four pre-specified high-risk subgroups.

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