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ORIGINAL RESEARCH

Factors Influencing Post-Myocardial Infarction Patients' Utilisation of Dual Antiplatelet Medication over the Long Term: Findings from the Tigris Registry

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ABSTRACT

Background: To outline the current patient profiles and treatment regimens, including antithrombotic care, for post-myocardial infarction (MI) stable coronary artery disease (CAD) patients from various geographical locations who are at high atherothrombotic risk.

Materials and Methods: 25 medical professionals (96% cardiologists) from india (2021-2022) enrolled patients 50 years old with prior MI 1-3 years ago and 1 risk factor (age 65, diabetes, second prior MI>1 yr ago, multivessel CAD, creatinine clearance 15–60 mL/min) in the prospective TIGRIS trial.

Results: 225 post-MI patients were enrolled (median 1.8 years): 52% with prior ST-elevation MI, median age 67, 24% women, 67% caucasian, 55% with 2 additional risk factors, 14% current smokers, 67% overweight/obese, 34% with blood pressure 140/90 mm Hg. 81% of MI patients had PCI (66% with drug-eluting stents). 75% of patients were discharged on dual antiplatelet treatment, mostly clopidogrel (75%). 63% had stopped antiplatelet therapy (1 year) on doctor's advice (90%). At enrollment, 97% were taking an antithrombotic medication, most commonly ASA (88%), with 27% on DAPT (median duration 1.6 years); highest (39%) in Asia-Pacific and lowest (12%) in Europe.

Conclusion: 1 in 4 post-MI patients didn't undergo DAPT for 1 year, despite guidelines. Contrary to guidelines favouring newer ADPris, clopidogrel was given. Prior to current RCT results supporting DAPT>1 year post-MI/PCI, >1 in 4 patients continued on DAPT, despite international variation.

Keywords: Antiplatelettherapy, myocardialinfarction, TIGRIS.

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INTRODUCTION

Coronary artery disease (CAD) is the leading cause of death around the world, and the number of people dying from it is growing because the population is growing and getting older, and because of changes in how diseases spread.[1] When a person has an acute coronary syndrome (ACS),[2-4] the early treatment and risks of death, myocardial infarction (MI), and stroke have been well studied, especially in people who took part in randomised clinical trials (RCTs).[5-7] But the later management of atherothrombotic risk factors, quality of life, and outcomes of a modern stable CAD (including post-MI) patient population from different geographic areas and non-RCT cohorts are less clear.[8–10] So, the Long Term Risk, Clinical

Management, and Healthcare Resource Utilization of Stable Coronary Artery Disease (TIGRIS) study was made to learn more about what happens to stable CAD patients 1–3 years after a MI in routine clinical practise. In particular, TIGRIS aims to provide up-to-date information on patient characteristics, treatment patterns, the burden of disease events like cardiovascular (CV) death, recurrent MI, stroke, and associated CV-related healthcare resource utilisation, as well as patient-reported quality of life from different geographical regions in an observational (real world) patient population at high atherothrombotic risk. The goal of these analyses was to describe how high atherothrombotic risk patients from different parts of the world are now being treated, including the dual antiplatelet therapy that is recommended by guidelines.[11]

MATERIALS AND METHODS

Stable CAD patients aged 50 or older having a documented history of presumed spontaneous MI, with their most recent MI happening 1 to 3 years before enrolling, providing informed written consent, and with at least 1 risk factor were included: (a) age 65; (b) medication-requiring diabetes; (c) documented history of a second suspected spontaneous MI (>1 year prior to enrolment); and/or (e) chronic, non-end stage renal impairment (Cockcroft Gault equation creatinine clearance 15 mL/min to 60 mL/min).

Exclusion criteria included: (a) presence of any condition/circumstance that could significantly limit patient follow-up; (b) presence of serious/severe co-morbidities that could limit life expectancy (1 year); (c) ongoing participation in a blinded randomized clinical trial where specific treatment(s) were not identifiable; and/or (d) patients receiving ticagrelor beyond 12 months post-MI (or off-label use of ticagrelor).

The study followed the Declaration of Helsinki, ICH Good Clinical Practice guidelines, and applicable regulations in participating countries. All participating sites' health authorities and ethics boards accepted the study protocol and informed consent.

Electronic case report form data entry (eCRF). Baseline data included pertinent medical history, demographics, details about the index MI that happened 1-3 years before inclusion, variables from routine physical examination and existing normal laboratory testing if completed within 3 months before and up to 1 month after the initial visit. The eCRF also recorded baseline medication use and healthcare resource use linked to CV or bleeding episodes in the 6 months before enrollment.

The EuroQol Research foundation survey instrument for measuring self-reported health status in 5 dimensions (EQ-5DTM; mobility, self-care, usual activities, pain or discomfort, anxiety or depression) was completed at the baseline visit.[12,13]

Most of the 349 recruiting physicians were cardiologists (n=334; 95.7%), internists (n=10; 2.8%), or other specialists (n=2; 0.6%), with a minority from general practise (n=3; 0.9%).[14]

TIGRIS is a descriptive observational research without explicit hypothesis testing. The sample size was initially estimated at 10,170 patients, assuming a 3-year event rate of 5-10%; this would allow the potential to describe an expected ischemic or bleeding event rate between 5% and 10% with a two-sided 95% confidence interval 0.4% and 0.6% from the observed proportions, respectively. Prospectively following patients for 2 years. The descriptive baseline analyses followed a framework. Frequencies and percentages express categorical data. Medians summaries continuous data (25th and 75th percentiles). A p-value 0.05 was considered significant, but multiple comparisons were not adjusted. SAS 9.4 and Enterprise Guide 6.1 were used for statistical analysis.[15]

RESULTS

Patient Population: 25 primary investigators from Asia-Pacific/Australia, Europe, North and South America enrolled 9,225 patients from June 18, 2020 to November 29, 2022. Eligible patients were 50 years or older, had a prior MI 1-3 years before inclusion in the registry, and

at least one additional risk factor (age 65 [62.5%], diabetes requiring medication [30.4%], second prior MI >1 year ago [10.2%], multivessel CAD [65.6%], chronic, non-end stage renal dysfunction [7.7%]). More than half of patients had 2 or more risk factors: 1 (44.8%), 2 (37.8%), 3 (14.0%), 4 (2.9%), and 5 (0.4%).

Table 1 includes patient demographics by region. The median age was 67 (25th, 75th percentiles: 60, 73), while 19.9% were 75 or older. 24.2% were women. Patients were mostly caucasian (66.6%), asian/oriental (27.5%), black (1.0%), and other (4.8%). At baseline, 14.0% smoked.

Table1: Selecteddemographicsandmedicalhistorybygeographicregion

	Totalpopulation	**India**	**Indonesia**	**Japan**	**China**
Number of patients	9225(100)	2850(30.9)	4240 (46.0)	1024 (11.1)	1111 (12.0)
Inclusion RiskFactors					
Age≥65years	5766(62.5)	1652(58.0)	2814 (66.4)	666 (65.0)	634 (57.1)
Diabetesrequiringmedication	2805(30.4)	999 (35.1)	1118 (26.4)	307 (30.0)	381 (34.3)
SecondPriorMI	943(10.2)	210(7.4)	491 (11.6)	131 (12.8)	111 (10.0)
MultivesselCAD	6052(65.6)	1921(67.4)	2714 (64.0)	715 (69.8)	702 (63.2)
CreatinineClearance 15-60ml/min	707(7.7)	212(7.4)	327(7.7)	78(7.6)	90(8.1)
Age,years*	67(60-73)	66(59-73)	68(62-73)	68 (61-74)	66 (59-73)
Women	2230(24.2)	616(21.6)	978(23.1)	320 (31.3)	316 (28.4)
Hypertension	6663(72.2)	1934(67.9)	3014 (71.1)	847 (82.7)	868 (78.1)
Hyperlipidemia	6147(66.6)	1386(48.6)	3024 (71.3)	927 (90.5)	810 (72.9)
Smokingstatus					
Currentsmoker	1288(14.0)	468(16.4)	595(14.0)	123 (12.0)	102(9.2)
Formersmoker	4482(48.6)	1194(41.9)	2201 (51.9)	505 (49.3)	582 (52.4)
Neversmoker	3453(37.4)	1187(41.7)	1443 (34.0)	396 (38.7)	427 (38.4)
DiabetesMellitus	3076(33.3)	1079(37.9)	1246 (29.4)	348 (34.0)	403 (36.3)
TypeI	88(2.9)	48(4.5)	29(2.3)	7 (2.0)	4 (1.0)
TypeII	2928(95.2)	989 (91.7)	1201 (96.4)	339 (97.4)	399 (99.0)
Unknown	60(2.0)	42(3.9)	16(1.3)	2 (0.6)	0 (0)
If type II-Management+					
Dietonly	253(8.6)	73(7.4)	119(9.9)	39(11.5)	22(5.5)
Oralhypoglycemic	2293(78.3)	812(82.1)	921(76.7)	226 (66.7)	334 (83.7)
Insulin	798 (27.3)	205(20.7)	359(29.9)	125 (36.9)	109 (27.3)
HistoryofPCI	7913(85.8)	2584(90.7)	3598	836	895

			(84.9)	(81.6)	(80.6)
HistoryofCABG	1314(14.2)	181(6.4)	663(15.6)	263 (25.7)	207 (18.6)
Chronicangina	90(1.0)	12(0.4)	54(1.3)	20(2.0)	4 (0.4)
Heartfailure	937 (10.2)	273(9.6)	472(11.1)	82(8.0)	110(9.9)
Atrialfibrillation	1061(11.5)	237(8.3)	569(13.4)	117 (11.4)	138 (12.4)
ICD	748(8.1)	150(5.3)	420(9.9)	133 (13.0)	45(4.1)
Pacemaker	198(2.2)	28(1.0)	104(2.5)	59(5.8)	7 (0.6)
TIA	211(2.3)	32(1.1)	131(3.1)	34(3.3)	14(1.3)
Stroke	204(2.2)	37 (1.3)	113(2.7)	39(3.8)	15(1.4)
Peripheralvasculardisease	413(4.5)	123 (4.3)	189(4.5)	58(5.7)	43(3.9)
Priorcerebrovascularrevascularization	616(6.7)	107(3.8)	358(8.4)	94(9.2)	57(5.1)
VTE	151(1.6)	26(0.9)	93(2.2)	25(2.4)	7 (0.6)
Valverepair/replacement	104(1.1)	13(0.5)	64(1.5)	16(1.6)	11(1.0)
COPD	670(7.3)	135(4.7)	384(9.1)	96 (9.4)	55(5.0)
Chronicanemia	272 (3.0)	54(1.9)	147(3.5)	49(4.8)	22(2.0)
Cancer	626(6.8)	124 (4.4)	330(7.8)	131 (12.8)	41(3.7)
Pepticulcer	298(3.2)	79(2.8)	167(3.9)	31(3.0)	21(1.9)
Severeliverdisease	36(0.4)	10(0.4)	19(0.5)	5 (0.5)	2 (0.2)
Esophagealvarices	18(0.2)	2 (0.1)	5 (0.1)	8 (0.8)	3 (0.3)
Majorbleeding#	261(2.8)	45(1.6)	138(3.3)	43(4.2)	35(3.2)

Allnumbersare given as numbers (%) ,except* median (25^{th},75^{th} percentiles), $^{+}$ Oral hypoglycemic agent(s) and insulin use are not mutually exclusive, CABG= Coronary Artery Bypass Graftsurgery; CAD= Coronary Artery Disease; COPD= Chronic Obstructive Pulmonary Disease; ICD= Implantable Cardioverter Defibrillator; PCI= Percutaneous Coronary Intervention; TIA=Transient Ischaemic Attack; VTE=VenousThromboembolism;# that required hospitalization or urgent medical care, and/or blood transfusion and/or causedhaematocritdrop. 4.0% had no formal education, 30.6% had 1-9 years, 31.5% had 10-12 years, 17.6% had 13-15 years, and 16.2% had 16 or more years. Most resided in a city (64.8%), 99% called home home, and 13.6% lived alone.

Most patients were retired (57.8%), with 25.6% working, 5.5% as homemakers, 4.9% jobless, and 4.4% on sick/disability leave. Half of the study group (n=4766, 51.7%) reported monthly household income less than or equal to $1,250, $1,251- $5,000, and >$5,000. Government (62.9%), private (19.4%), employer-provided (3.5%), other (4.8%), and none (5.5%) were among the 98.7% of patients who replied.

Infarction: 1.8 (1.3, 2.4) years passed between the index MI and study enrollment. ST-segment elevation MI (STEMI) was 52.1%, non-ST-segment elevation MI (NSTEMI) was 41.8%, and 6.1% was unknown. PCI (80%), CABG (7.4%), or medical treatment (12.6%) was used to treat the index MI (Table 2). Compared to NSTEMI patients, more STEMI patients underwent PCI (71.9% vs. 88.0%); fewer STEMI patients underwent CABG (11.6% vs. 3.6%) or got medical therapy only (16.5% vs. 8.4%).

Table 2: Coronary revascularization during the index myocardial infarction bygeographicalregion

	Totalpopulation	**India**	**Indonesia**	**Japan**	**China**
Numberofpatients	9225(100)	2850(30.9)	4240(46.0)	1024(11.1)	1111 (12.0)
PercutaneousCoronaryIntervention	7376(80.0)	2472(86.7)	3358(79.2)	747(72.9)	799(71.9)

Drug-ElutingStent	4146(56.2)	1750(70.8)	1753(52.2)	414(55.4)	229(28.7)
BareMetalStent	1476(20.0)	267(10.8)	730(21.7)	159 (21.3)	320(40.1)
Bothstenttypes	59(0.8)	13(0.5)	34(1.0)	9 (1.2)	3 (0.4)
Nostent	207 (2.8)	42(1.7)	118(3.5)	19(2.5)	28(3.5)
Unknown/incompletetype	1488(20.2)	400 (16.2)	723(21.5)	146(19.5)	219(27.4)
Coronary arterybypasssurgery	678(7.4)	98(3.4)	332(7.8)	143(14)	105(9.5)

Allnumbersaregivenasnumbers(%)

Physical and Laboratory Findings: Supplemental [Table 1] lists baseline physical exam findings by region. 43.4% were overweight and 24.2% were obese (median BMI: 27 kg/m2). Median waist circumference: 97 cm. Asia-Pacific had the lowest obesity rate and waist circumference.

Asia-Pacific had the greatest resting heart rate, 68 beats/minute. The European region had the highest baseline systolic BP; 29% with a history of hypertension and 18.9% without had a blood pressure 140/90 mm Hg.

Laboratory Values: In 2,810 individuals with routine laboratory testing (3 months before or 1 month after the initial visit), serum haemoglobin was 13.9 (12.8, 15.0) g/dL. Serum creatinine in 3,285 patients was 0.97 (0.83, 1.17) mg/dL; 2.5% had a creatinine clearance (CrCl) of 30 ml/min/1.73 m2, 19.2% had a CrCl of 30-60 ml/min/1.73 m2, and 78.4% had a CrCl of >60 ml/min/1.73 m2. Fasting glucose was 106 (94, 127) mg/dL (n=2,034) and haemoglobin A1c was 6.3 (5.8, 7.0) % (n=1,565), including among diabetics: 132 (111, 164) mg/dL (n=731) and 6.9 (6.4, 7.7) % (n=821). Total cholesterol (n=2.954), fasting LDL (n=2.027), HDL (n=2.871), and fasting triglycerides (n=2.123) were 151 (131, 176), 78 (63, 99), 45 (38, 54), and 115 (86, 157) mg/dL, respectively. 37% had fasting LDL 70 mg/dL.

Antithrombotic Therapy: Single antiplatelet therapy was prescribed in 21.3% (ASA 14.5%, ADP receptor inhibitor 6.8%), dual antiplatelet therapy in 74.9% (clopidogrel 55.8%, prasugrel 10.7%, ticagrelor 7.9%, or ticlopidine 0.1%), and oral anticoagulant medication in 5.5%.

Other Medical Therapy:

Table 4 lists other medical medications at enrollment, including beta-blocker (79.9%), ACE inhibitor (47.9%), ARB (29.2%), statin (92.8%), other lipid-lowering (9.4%), diuretic (25.4%), and antidepressant (7.0%) therapy. India used beta-blockers the most (86.7%), while Indonesia used the fewest (70.9%). In Japan (80.9%) and China (71.5%), ACE or ARB use was highest. Statin use was high (92%) in all regions, although alternative lipid-lowering therapy was highest in North America (15.6%). Among 2,805 diabetics, 81.8% had Type II and 28.5% had Type I.

Health Care Resource Utilization and Status:

In the 6 months before enrollment, 31.7% of participants saw a cardiologist, 7.7% a specialist, 19.6% a family doctor, and 5.8% an emergency room. 5.4% of hospitalizations in the past 6 months were for cardiovascular (4.8%) or bleeding (0.7%) events (including coronary angiography), with a median stay of 4 (2, 7) days.

Self-reported health status by EQ-5D evaluation was available at baseline in 9,177 (99.5%) patients. Mobility (24.7%), self-care (5.8%), regular activities (18.5%), pain/discomfort (36.0%), and anxiety/depression (22.8%) were limits. Overall health status was 0.85 on the EQ-Index and 80 on the EQ-VAS (scale from 1-100).

DISCUSSION

This research provides unique contemporary enrollment data on patient characteristics, treatment patterns, CV-related healthcare resource consumption, and quality of life in stable high-risk CAD patients 1-3 years post-MI in routine clinical practise. 1 in 7 MI patients are current smokers, 2 in 3 are overweight or obese, and 1 in 4 had blood pressure 140/90 mm

Hg.[16] Almost all patients used at least one antithrombotic medicine, a statin, and/or lipid-lowering therapy, and 8 in 10 took a beta-blocker plus an ACE inhibitor or ARB. 1 in 4 post-MI patients with 1 atherothrombotic risk factor didn't receive DAPT for 1 year. Contrary to randomised clinical trial data and international guideline recommendations, clopidogrel was largely administered as part of DAPT.[17] Prior to current randomised trial findings supporting DAPT >1 year post-MI/PCI, >1 in 4 patients persisted on DAPT, with worldwide variation.[18] 1 in 5 patients saw a doctor or ER in the 6 months before enrollment, and 1 in 20 were hospitalised for a CV or bleeding incident. Despite challenges with mobility (25%), self-care (5%), typical activities (19%), pain/discomfort (36%), and anxiety/depression (23%), overall health status is similar to that in an age- and sex-matched U.K. population without cardiovascular disease.[19-21]

While the study includes patients at least 50 years old with additional high risk features, such as age 65 (63%, with 20% 75), multivessel disease (66%), diabetes mellitus requiring medication (30%), a second prior MI >1 year ago (10%), or chronic, non-end stage renal dysfunction (8%), more than half (55%) have more than one of the qualifying, prognostically important factors. The senior demographic (median 67) certainly accounts for 62% of retired or sick/disabled.[22] Higher proportions of STEMI patients (52%) and those who received coronary revascularization (88%) presumably reflect the fact that most recruiting physicians were cardiologists. Similarly, most of the TIGRIS population lives in an urban location (65%) and earns $15,000 U.S. annually (51%).[23] Lower rates of obesity in India compared to other locations, and lower rates of antithrombotic treatments and beta-blockers, but higher rates of DAPT >1 year post-MI.[24] Europe used more ACE inhibitors and ARBs than North America. The larger use of previous PCI in indiamay explains the continued use of DAPT.[25] Despite 93% of these patients receiving statin and/or other lipid-modifying therapy, 60% of patients had LDL-cholesterol over some (but not all) international guideline-recommended target(s).[26] Consistent with international guideline recommendations and an earlier prospective observational international study of ACS hospital survivors, 75% of patients received dual antiplatelet therapy (DAPT) as part of their index MI management, especially in the setting of frequent PCI with stenting, for approximately 1 year post. Contrary to guideline guidelines and RCT evidence supporting the superiority of prasugrel or ticagrelor, clopidogrel was recommended.[27,28] Before more recent RCT results supporting DAPT beyond 1 year post-MI/PCI with stenting, 27% of our cohort were on DAPT for at least 1.6 years until TIGRIS enrollment.[29,30]

CONCLUSION

In a large worldwide population, atherothrombotic risk factor modification (smoking, obesity, hypertension, dyslipidemia) is poor 2 years after a MI. Most patients received evidence-based pharmacological therapy, including antithrombotic, beta-blocker, ACE inhibitor, and statin medication (s). Despite concerns with self-reported quality of life, this population's overall health status was high. Consistent with guidelines, patients got DAPT for 1 year post-MI; however, clopidogrel was largely administered post-index MI. More than 1 in 4 patients have continued DAPT >1 year post-MI/PCI, despite international variation. These findings could improve antithrombotic treatment for post-MI patients.

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