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CLINICAL RESEARCH

Impact of the Lubrizol factory fire in Rouen on coronary events: A retrospective study from the France PCI registry☆

Impact de l'incendie Lubrizol à Rouen sur les évènements coronariens : étude rétrospective à partir du registre France PCI

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Abbreviations: ACS, acute coronary syndrome; ARMA, autoregressive moving average; CCS, chronic coronary syndrome; CI, confidence interval; COVID-19, coronavirus disease 2019; France PCI, France Percutaneous Coronary Intervention; NSTEMI, non-ST-segment elevation myocardial infarction; STEMI, ST-segment elevation myocardial infarction.

☆ Tweet: On 26 September 2019, a fire occurred in the Lubrizol factory in Rouen (France). Thanks to the FRANCE-PCI registry, we evaluated its impact on the incidence of coronary artery events. Our study did not find a significant increase in the incidence of acute coronary syndrome.

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KEYWORDS
Coronary artery disease;
Acute coronary syndrome;
Industrial fire

Summary
Background. — On 26 September 2019, an industrial fire occurred in the Lubrizol factory in Rouen (France), exposing the population to the inhalation of many volatile toxic agents secondary to combustion.
Aim. — To assess the impact of the Lubrizol factory fire on the incidence of coronary artery events.
Methods. — All coronary angiograms performed in Rouen (exposed) and Le Havre (unexposed) from May 2019 to December 2019 were extracted from the prospective France Percutaneous Coronary Intervention (France PCI) registry. To study the impact of the fire on coronary events, an interrupted time series analysis was performed in Rouen, with adjustment on Le Havre in an autoregressive moving average (ARMA)(1,1) model with the precision of 1 week. The primary outcome was the incidence of acute coronary syndrome, and the secondary outcome was the incidence of ST-segment elevation myocardial infarction.
Results. — The mean number of acute coronary syndromes per week in the exposed zone (Rouen) increased non-significantly from 37.5 ± 9.4 before the fire to 43.2 ± 6.2 after the fire, for an estimated effect of +5.5 (95% confidence interval −0.7 to 11.8; $P = 0.09$) events per week. In municipalities exposed to the plume of smoke (subgroup of Rouen), the mean number of acute coronary syndromes increased non-significantly from 7.3 ± 2.8 before the fire to 8.7 ± 3.6 after the fire, for an estimated effect of +1.0 (95% confidence interval −2.0 to 4.0; $P = 0.51$) events per week. The results were similar when taking into account only ST-segment elevation myocardial infarctions or all coronary events.
Conclusions. — Our study did not find a significant effect of the Lubrizol factory fire on the incidence of acute coronary syndrome. Further studies are needed to investigate the impact of industrial accidents on air pollution and coronary events.

MOTS CLÉS
Insuffisance coronaire ;
Syndrome coronaire aigu ;
Incendie industriel

Résumé
Contexte. — Le 26 septembre 2019, un incendie industriel s'est déclaré dans l'usine Lubrizol à Rouen (France), exposant la population à l'inhalation de nombreux agents toxiques volatils secondaires à la combustion.
Objectif. — Évaluer son impact sur l'incidence des événements coronariens aigus.
Méthodes. — Toutes les coronarographies réalisées à Rouen (zone exposée) et au Havre (zone non exposée) de janvier 2019 à décembre 2019 ont été extraites du registre prospectif France PCI. Pour étudier l'impact de l'incendie sur les événements coronariens, une analyse de séries temporelles interrompues a été réalisée à Rouen, avec ajustement sur Le Havre dans un modèle ARMA(1,1) avec une précision d'une semaine. Le critère de jugement principal était l'incidence des évènements coronariens aigus et le critère de jugement secondaire était l'incidence de l'infarctus du myocarde avec élévation du segment ST.
Résultats. — Le nombre moyen d'événements coronariens aigus par semaine en zone exposée (Rouen) a augmenté non significativement de $37,5 \pm 9,4$ avant l'incendie à $43,2 \pm 6,2$ après l'incendie, pour un effet estimé de +5,5 (IC95 % −0,7 à 11,8 ; $p = 0,09$) événements par semaine. Dans les communes exposées au panache de fumée (sous-groupe de Rouen), le nombre moyen d'événements coronariens aigus a augmenté de façon non significative de $7,3 \pm 2,8$ avant l'incendie à $8,7 \pm 3,6$ après l'incendie pour un effet estimé à +1,0 (IC95 % −2,0 à 4,0; $p = 0,51$) événements par semaine. Les résultats étaient similaires en ne prenant en compte que les infarctus du myocarde avec élévation du segment ST ou l'ensemble des évènements coronariens.
Conclusions. — Notre étude n'a pas retrouvé d'effet significatif de l'incendie de l'usine Lubrizol sur l'incidence des événements coronariens aigus. D'autres études sont nécessaires pour étudier l'impact des accidents industriels sur la pollution de l'air et les événements coronariens.

Background

Over the last decade, a growing body of epidemiological and clinical evidence has led to heightened concern regarding the impact of pollution on cardiovascular disease. Atmospheric pollutants are a heterogeneous group of particles, because of their size, composition and origin. Fine particles (< 2.5 μm) are ubiquitous in cities and urban areas; they are mainly emitted during combustion of diesel and gasoline, but also during multiple industrial processes. The half-life of these fine particles is a few days, and they can spread over several kilometres [1,2]. On Thursday 26 September 2019, a fire occurred in the Lubrizol factory in Rouen (Normandy, France), exposing 112 surrounding municipalities to the inhalation of numerous toxic agents (Fig. 1 and Fig. 2); some of these agents are not yet characterized. The Lubrizol factory manufactures additives and lubricants; because of the toxic nature of the chemicals it produces, the Lubrizol site is covered by the Seveso-III Directive. During this fire, 9,419 tons of products burned. According to the National Institute for the Industrial Environment and Risks, there were 617 referenced products, mainly multiuse and control additives, composed of oils, mineral oils, sulfur derivatives of hydrocarbons, chlorinated products and several tons of tyres and arabic gum in storage; this explains the presence of polychlorinated dioxins, polychlorofurans, aldehydes and mercaptans in the smoke from this fire.

To our knowledge, no study has evaluated the impact of the Lubrizol fire on the occurrence of coronary events in Rouen and its surrounding areas. The aim of this retrospective multicentre study was to assess the impact of the Lubrizol factory fire in Rouen on the incidence of coronary events.

Methods

All coronary angiograms performed between 01st May 2019 and 31st December 2019 in France were recorded prospectively in the France Percutaneous Coronary Intervention (France PCI) registry. France PCI is a French national registry that aims to identify coronary and angioplasty activities in France. More than 150 epidemiological, clinical and procedural variables are included in the database. These data are extracted from the reporting software (CardioReport, MediReport, Paris, France), and are monitored to ensure the absence of erroneous data and good completeness.

Figure 1. Image of the Lubrizol fire in Rouen on 26 September 2019.

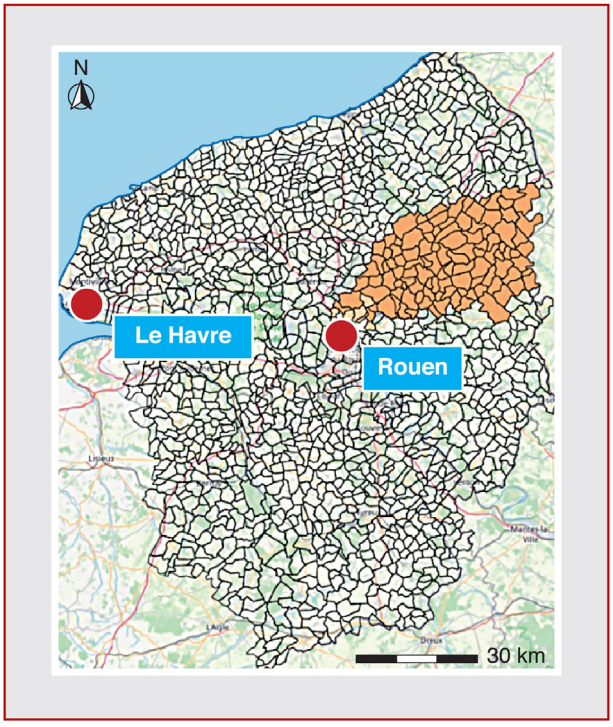


Figure 2. Map of the 112 municipalities in the North-East of Rouen exposed to the plume of smoke from the Lubrizol fire.

Definition of geographical zones

The France PCI registry has been used by all interventional cardiology centres ($n = 4$) in the Seine-Maritime department (Normandy region) since May 2019, allowing an exhaustive collection of all coronary angiography and/or percutaneous coronary intervention procedures performed for the evaluation and management of coronary artery disease. An interrupted times series was analysed to evaluate the impact of the fire on coronary syndromes. The period before the Lubrizol fire was defined as 01st May (the date on which the four centres started participating in the registry) to 25th September 2019, and the period after the fire was defined as 26th September to 31st December 2019. Two centres (CHU Rouen and Clinique Saint-Hilaire) were in the target zone (Rouen and surrounding areas), whereas two centres (*Groupe Hospitalier du Havre* and *Hôpital Privé de l'Estuaire*) were in an unexposed control zone (Le Havre and surrounding areas). Le Havre is located about 100 km from Rouen, and was not exposed to the plume of smoke (Fig. 2). The two geographical zones are far enough apart to avoid competition of activity between the centres of Le Havre and Rouen, except for a small overlapping zone.

Inclusion/exclusion criteria

Patients who had a coronary angiogram in one of the four centres of the study, from 01st May to 31st December 2019, were included if the indication for coronary angiography was a coronary event, defined as follows: acute coronary syndrome (ACS) with ST-segment elevation (ST-segment elevation myocardial infarction [STEMI]) or without ST-segment elevation (non-ST-segment elevation myocardial infarction [NSTEMI], unstable angina); cardiac arrest related to an ACS; and chronic coronary syndrome (CCS).

Patients who had coronary angiography for another reason were not included in the present study.

Outcomes

The primary outcome was the incidence rate of all acute coronary events. The secondary outcomes were the incidence rates of STEMI and of all coronary events, including ACS and CCS. A similar analysis was performed in the 112 municipalities exposed to the plume of smoke (Fig. 2).

Variables collected

In addition to centre and outcome, the residential postcodes of patients were also collected, to refine the analysis according to the plume of smoke that spread over the region. Indeed, 112 municipalities were identified as being exposed to this cloud of smoke in the greater Rouen area (Fig. 2). Furthermore, coronary events during the period from May to December 2020 were also recorded.

Statistical analysis

The time series was based on the weekly number of coronary events in the two centres of Rouen and the two centres of Le Havre. Because of the presence of external factors, such as air pollution, that may change the risk of coronary events in the whole population at once, the assumption of independence of events of the Poisson distribution may be violated. This violation has two consequences. First, the between-weeks variance of incidence is greater than would be expected with a Poisson distribution (overdispersion). Second, the incidence of coronary events in two successive weeks is correlated (autocorrelation). The autoregressive moving average (ARMA) models, classically used in time series, empirically estimate these two effects, avoiding the underestimation of sampling fluctuations and inflation of type I error rate that the Poisson regression would have. An ARMA(p,q) model uses a number p of parameters to describe the autocorrelation, a number q of parameters to describe the relationship between the incidence and the average incidence in previous weeks, and a residual variance parameter incorporating the overdispersion.

In order to take into account a possible seasonal effect shared by Rouen and Le Havre, the primary analysis was done in an ARMA(1,1) model, explaining the weekly number of coronary events in Rouen by the period (before or after), and the weekly number of coronary events in Le Havre. As the fire occurred on a Wednesday, this day became the first day of all weeks analysed, and Tuesday became the last day of all weeks analysed. Several sensitivity analyses were performed: removing the adjustment of Le Havre; using an ARMA(2,2) model; using an ARMA(1,0) model; and using an ARMA(0,0) model. A graphical analysis of partial autocorrelation coefficients with lag 1 to 14 was done to assess the validity of the ARMA(1,1) model. Validity of the normal approximation was guaranteed by the large sample size and expected moderate autocorrelation and overdispersion; normality Q-Q plots confirmed this expectation.

Secondary analyses, mimicking the primary analysis with different outcomes, included: (1) a subgroup analysis in municipalities under the plume of smoke; (2) an analysis restricted to STEMI; and (3) a post hoc analysis of all ACSs.

With data on the coronary events 1 year later (2020), an analysis adjusted on the seasonal effect was performed: after numbering weeks from −21 to +13, relative to the day of the fire in 2019 or the day of the anniversary of the fire in 2020, paired differences of 2019 minus 2020 were calculated. These paired differences can be interpreted as the excess number of events in 2019 compared with 2020 in the same week. An ARMA(1,1) model explaining the weekly excess number of coronary events in 2019 in Rouen was estimated, with an adjustment on the weekly excess number of coronary events in Le Havre in 2019. Seasonal effects were also evaluated in 2020 in Rouen and Le Havre, by testing the effect of the binary variable before/after the day of the anniversary of the fire.

Quantitative variables are described as mean ± standard deviation or median (interquartile range), according to their distribution. Categorical variables are described as percentages. Comparison of quantitative variables was performed using Student's t-test or analysis of variance (ANOVA) if the normal approximation was acceptable, or a Mann–Whitney test or Kruskal–Wallis test otherwise. Categorical and ordinal variables were compared with the use of Fisher's exact test or the Chi^2 test. Differences were considered statistically significant if P was < 0.05. The statistical analysis was carried out using R software (R Foundation for Statistical Computing, Vienna, Austria).

Results

Out of 6,380 procedures recorded in the France PCI registry during the study period, 3,367 (53%) were associated with a coronary event, according to our definition. The flow chart is shown in Fig. 3.

Characteristics of coronary events before and after the Lubrizol fire in Rouen and in Le Havre

The median age of the 3,367 patients with coronary events in 2019 was 68.0 (58.0–77.0) years, and the majority were men (69.8%). The baseline characteristics of the studied population and procedural characteristics in Rouen (exposed zone) are shown in Table 1 (ACS) and Online material Table A.1 (all coronary events). There was no significant difference between the characteristics of patients in Rouen before versus after the Lubrizol fire, except for the proportion with a family history of coronary artery disease. In Le Havre (unexposed control zone) in 2019, there were significantly

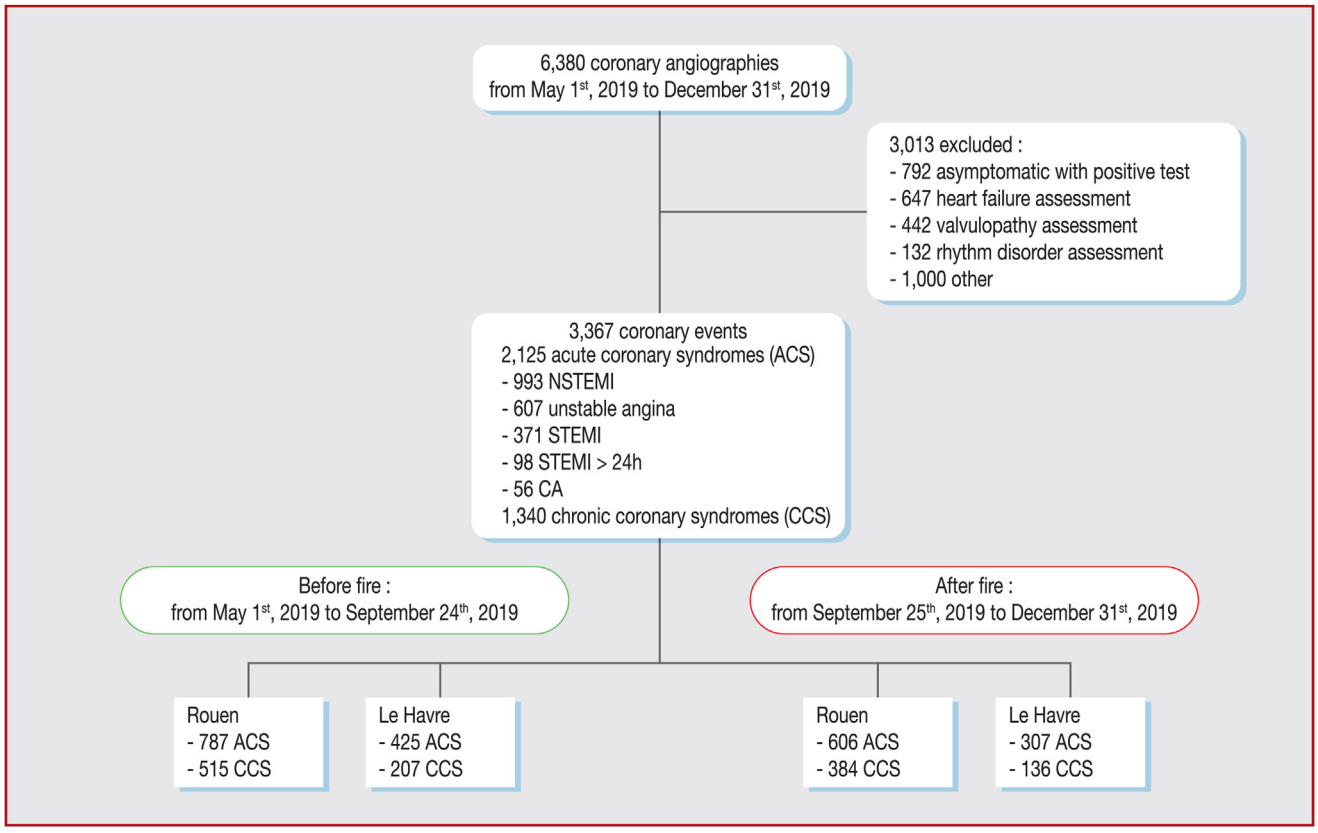
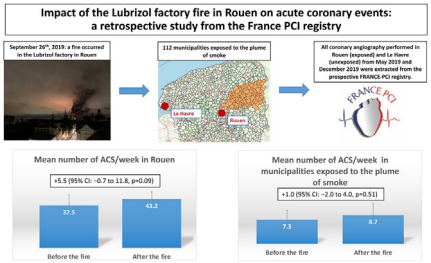


Figure 3. Flow chart. ACS: acute coronary syndrome; CA: cardiac arrest; CCS: chronic coronary syndrome; NSTEMI: non-ST-segment elevation myocardial infarction; STEMI: ST-segment elevation myocardial infarction.

more patients with dyslipidaemia in the period after the fire (50.3% vs 42.6%; $P = 0.015$; Online material Table A.2).

Primary analysis

The mean number of all ACS events per week in the exposed zone (Rouen) increased non-significantly from 37.5 ± 9.4 before the fire to 43.2 ± 6.2 after the fire, for an estimated effect of +5.5 (95% confidence interval [CI] — 0.7 to 11.8; $P = 0.09$) events per week in the ARMA(1,1) model adjusted on Le Havre (Central illustration



); in Le Havre, this increased from 20.3 ± 5.2 to 21.8 ± 4.7, for an estimated effect of +1.4 (95% CI — 2.3 to 5.1; $P = 0.46$) in an ARMA(1,1) model without adjustment.

Sensitivity analyses

The difference in the number of all ACS events per week was consistent with the primary analysis in sensitivity analyses: +4.8 (95% CI — 2.6 to 12.1; $P = 0.21$) coronary events per week in an ARMA(2,2) model; +5.5 (95% CI — 0.8 to 11.8; $P = 0.10$) in an ARMA(1,0) model; and +5.7 (95% CI — 0.3 to 11.7; $P = 0.07$) when removing the adjustment on the incidence in the unexposed zone (Le Havre) from the model. A last sensitivity analysis, based on a naïve variance estimator, ignoring the autocorrelation, i.e. ARMA(0,0) model, showed an increase estimated at +5.6 (95% CI — 0.1 to 11.4; $P = 0.06$).

Secondary analyses

STEMI events

The mean number of STEMI events per week in the exposed zone (Rouen) increased non-significantly from 6.2 ± 3.0 before the fire to 7.9 ± 3.6 after the fire, with a difference estimated at +1.8 (95% CI —0.5 to 4.1; $P = 0.13$) in an ARMA(1,1) model adjusted on the incidence of STEMI events in Le Havre. In Le Havre, the mean number of STEMI events increased from 3.2 ± 1.8 to 4.4 ± 2.2, with a significant increase in the second period (+1.2 events/week, 95% CI 0.2 to 2.2; $P = 0.02$); contrary to other models having positive estimates of autocorrelation coefficients (phi or theta), this one found a slightly negative estimate of the moving-average coefficient (phi = —0.16) and the autocorrelation coefficient (theta = —0.096); excluding autocorrelation terms (post hoc sensitivity analysis), the difference was no longer significant (+1.2 events/week, 95% CI —0.1 to 2.5; $P = 0.09$).

Table 1 Population and procedural characteristics of acute coronary syndromes in Rouen in 2019.

	Before fire	After fire	*P*
	(*n* = 787)	(*n* = 606)	
Age (years)	67.0 (57.0—79.0)	67.0 (57.0—75.0)	0.58
Male sex	556 (70.7)	426 (70.5)	0.98
Hypertension	450 (57.8)	331 (55.2)	0.35
Current smoker	193 (24.8)	146 (24.6)	0.99
Dyslipidaemia	378 (48.9)	303 (50.9)	0.49
Diabetes	193 (24.8)	157 (26.3)	0.56
Family history of CAD	163 (21.2)	86 (14.5)	0.002
BMI (kg/m^2)	27.2 (24.6—30.4)	27.1 (24.5—30.8)	0.67
History of myocardial infarction	94 (12.0)	89 (14.9)	0.14
History of peripheral artery disease	78 (10.0)	50 (8.3)	0.33
History of stroke	30 (3.8)	30 (5.0)	0.37
Renal failure	60 (7.7)	54 (9.0)	0.44
History of PCI	207 (26.4)	156 (26.0)	0.90
History of CABG	38 (4.8)	28 (4.6)	0.96
Radial access	685 (87.0)	541 (89.3)	0.23
Duration of scopy per procedure (minutes)	6.6 (3.5—11.3)	6.5 (3.4—11.2)	0.78
Indication for coronarography			0.71
STEMI	130 (16.5)	111 (18.3)	—
NSTEMI	368 (46.8)	279 (46.0)	—
Cardiac arrest	21 (2.7)	18 (3.0)	—
Unstable angina	220 (28.0)	170 (28.1)	—
STEMI > 24 hours	48 (6.1)	28 (4.6)	—
Coronarography result			0.68
Normal	75 (9.5)	59 (9.7)	—
Lesion < 50%	52 (6.6)	44 (7.3)	—
Monotroncular	264 (33.5)	189 (31.2)	—
Bitroncular	215 (27.3)	184 (30.4)	—
Tritroncular	181 (23.0)	130 (21.5)	—
Left main coronary lesion > 50%	64 (8.1)	40 (6.6)	0.33
CABG lesion > 50%	22 (2.8)	13 (2.1)	0.55
Syntax score per procedure	10 (6—17.5)	9 (5—15)	0.14
Treatment			0.48
No treatment	50 (6.4)	26 (4.4)	—
Medical	170 (21.7)	139 (23.6)	—
PCI	476 (60.8)	367 (62.2)	—
Medical/surgical staff or CABG	74 (9.5)	50 (8.5)	—
Other	13 (1.7)	8 (1.4)	—
Number of PCIs per procedure	0.81 ± 0.89	0.74 ± 0.84	0.17
Number of stents implanted per procedure	0.80 ± 0.92	0.77 ± 0.94	0.56

BMI: body mass index; CABG: coronary artery bypass graft; CAD: coronary artery disease; PCI: percutaneous coronary intervention; NSTEMI: non-ST-segment elevation myocardial infarction; STEMI: ST-segment elevation myocardial infarction. Data are expressed as median (interquartile range), number (%) or mean ± standard deviation.

All coronary events

The numbers of overall coronary events per week before and after the fire in the exposed zone (Rouen) and in the unexposed control zone (Le Havre) are shown in Fig. 4A and C. In the 21 weeks preceding the Lubrizol fire, there were a mean 62.0 ± 10.1 coronary events per week in the exposed zone (Rouen). In the 14 weeks following the fire, there were a mean 70.6 ± 10.5 coronary events per week in the exposed zone (Rouen). The difference in the number of overall coronary events per week was estimated at +5.5 (95% CI − 6.0 to 16.9; *P* = 0.36) between periods in an ARMA(1,1) model with adjustment on Le Havre. In Le Havre, there were a mean 30.2 ± 6.3 coronary events per week before the Lubrizol fire and 31.5 ± 5.9 coronary events after the Lubrizol fire. The unadjusted difference in the number of overall coronary events per week was estimated at +1.0 (95% CI − 4.1 to 6.1; *P* = 0.71) in Le Havre.

Municipalities exposed to the plume of smoke

Among the 3,367 coronary events of 2019, the postcode was missing for 65 (1.9%) of them. There were 2,838 (86%) events in areas not exposed to the plume of smoke, and 464 (14%) events in exposed areas (112 municipalities). Two hundred and sixty-two patients had a coronary event, including 51

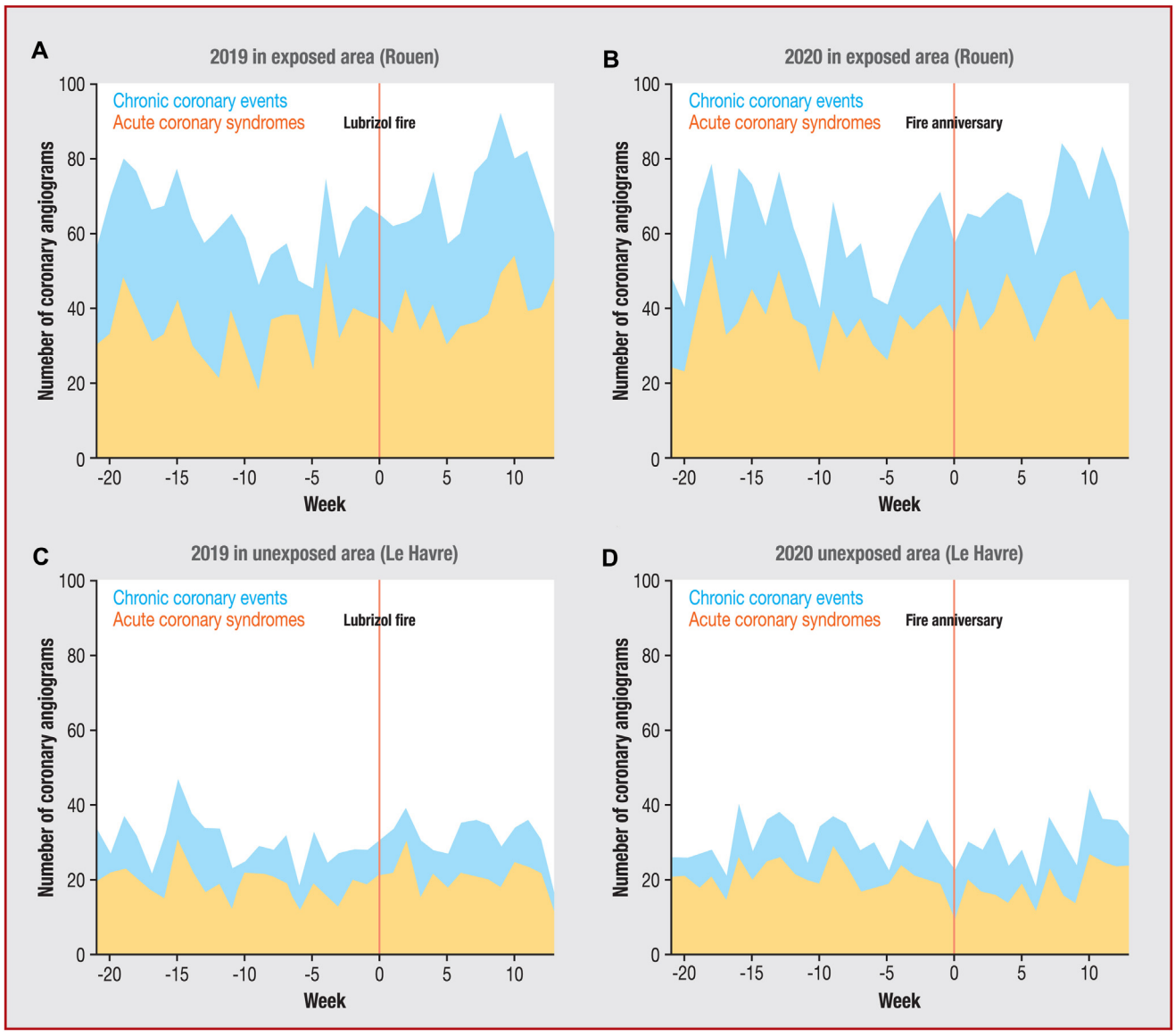
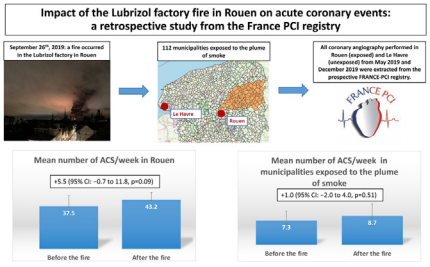


Figure 4. A and C. Graphs showing the number of acute (red) and chronic (blue) coronary events per week before and after the fire in Rouen (A) and Le Havre (C). B and D. Graphs showing the number of coronary events per week in Rouen (B) and Le Havre (D) before and after the fire anniversary in 2020.

cases of STEMI in exposed areas. In municipalities exposed to the plume of smoke (subgroup of Rouen), the mean number of ACSs increased non-significantly from 7.3 ± 2.8 before the fire to 8.7 ± 3.6 after the fire, for an estimated effect of +1.0 (95% CI—2.0 to 4.0; $P = 0.51$) events per week in an ARMA(1,1) model adjusted on the incidence in Le Havre (Central illustration 

). Moreover, the mean number of STEMI events increased non-significantly from 1.4 ± 1.2 before the fire to 1.5 ± 1.3 after the fire, for an estimated effect of +0.2 (95% CI − 1.0 to 1.5; $P = 0.74$) events per week in an ARMA(1,1) model adjusted on the incidence in Le Havre.

Finally, the mean number of overall coronary events increased non-significantly from 12.2 ± 3.7 before the fire to 14.9 ± 4.1 after the fire, for an estimated effect of +2.2 (95% CI—0.8 to 5.2; $P = 0.16$) events per week in an ARMA(1,1) model adjusted on the incidence in Le Havre.

Post hoc analysis with correction on the seasonal effect of 2020

In Rouen, the mean weekly number of acute coronary events was 37.6 ± 8.3 from May to December 2019 and 38.6 ± 7.6 from May to December 2020 (Fig. 4B and Fig. 4D). In Le Havre, the mean weekly number of coronary events was 20.3 ± 4.6 in 2019 and 20.5 ± 4.5 in 2020. The mean weekly number of all coronary events was 65.5 ± 11.0 from May to

December 2019 and 62.8 ± 12.1 from May to December 2020. In Le Havre, the mean weekly number of coronary events was 30.7 ± 6.1 in 2019 and 30.4 ± 5.9 in 2020.

The seasonal effect on year 2020 in the exposed area (Rouen) was estimated as a non-significant increase of +4.4 (95% CI −1.3 to 10.1; $P = 0.14$) ACSs and +8.6 (95% CI −0.7 to 17.9; $P = 0.08$) all coronary events in the period after the fire anniversary compared with the period before the fire anniversary. In Le Havre, the seasonal effect was estimated at −4.4 (95% CI −10.7 to 1.8; $P = 0.17$) and −0.3 (95% CI −6.2 to 5.6; $P = 0.92$) for ACSs and all coronary events, respectively. In the model with correction of the seasonal effect by the paired weekly differences in the number of acute coronary events in 2019 minus 2020, the number of ACSs in Rouen with adjustment on Le Havre did not increase significantly after the fire (+0.1 events/week, 95% CI −9.7 to 9.9; $P = 0.99$). Similar results were obtained for all coronary events (−1.4 events/week, 95% CI −7.4 to 4.7; $P = 0.66$).

Discussion

The question of the health risk secondary to a plume of smoke from a fire has been the subject of much public debate. To our knowledge, our work is the only one that has investigated the impact of the Rouen Lubrizol fire on coronary events. It was legitimate to hypothesize that the Rouen Lubrizol fire could have an effect on the occurrence of ACS, as several studies had found an association between air pollution, exposure to fine particles and ACS [3,4]. The main chemical components incriminated are carbon monoxide, nitrogen dioxide and sulfur dioxide [5]. Various mechanisms may be involved in the occurrence of coronary events. Indeed. it has already been demonstrated that exposure to fine particles increases fibrinogen concentration and platelet activation, thus promoting intravascular thrombosis and ACS [6,7]. Likewise, these pollutants, by creating endothelial dysfunction, lead to the phenomena of vasoconstriction, loss of vascular regeneration capacities and destabilization of atheromatous plaques [8,9].

The objective of this retrospective study was to assess the impact of a large industrial fire (at the Lubrizol factory in Rouen) on the incidence of coronary events. The study exhaustively collected all the coronary events leading to a coronary angiogram from the France PCI registry, in which four interventional cardiology centres of the region have participated since 01 May 2019. We did not find a significant difference between groups in the primary analysis, taking into account the autocorrelation and possible seasonal effect by adjustment on a control zone. Similarly, we did not observe a significant variation in the number of ACSs in the 112 municipalities exposed to the plume of smoke. The adjustment on a possible seasonal effect was important, because an increase in ACSs in winter has been described previously [10]. For several days, or even weeks, fumes could be smelt in the city. It is therefore possible that the fire had not only a one-off effect but also a delayed effect linked to persistent exposure. This potential delayed effect may not be detectable because of lack of statistical power. Furthermore, more precise analysis from municipalities exposed to the plume of smoke did not find any significant difference either. This analysis based on the residential postcode may be biased, because it did not take into account the movements of the population during the study period.

Very few studies have analysed the impact of industrial accidents on coronary events. Although the two industrial disasters are different, a similar study was performed after the explosion of the AZF factory (Toulouse, France) in 2001 [11]. This study reported a sudden increase in ACSs. During this accident, a large explosion occurred, but the population was not exposed to a plume of smoke such as that in Rouen. The authors hypothesized that the increase in ACSs was not related to exposure to toxic agents, but to emotional stress induced by this explosion a few days after the terrorist attacks of 11 September 2001 [12]. The emotional component is therefore not comparable in intensity with the Lubrizol factory fire.

Regardless, we believe it is important to continue to assess the potential impact of industrial disasters on coronary events. Interestingly, on 14 June 2021, a similar fire and explosion occurred in Rocktown (IL, USA), with a plume of smoke comparable to the Lubrizol fire in Rouen. The authorities in the USA took the precaution of evacuating the population within a 1.6 km perimeter, which was not the case in Rouen. It would be interesting to assess the impact of this fire on coronary events in the surrounding area, and to combine them with our analysis, because the pollutants were similar, and our study may be underpowered to detect an effect.

Limitations and perspectives

This study has several limitations. As with any retrospective study, there may be confounding factors that might bias results. First, the study periods before (1st May to 25th September) and after (26th September to 31st December) are not comparable, and the choice of study period was purely arbitrary, because the France PCI registry did not cover the entire region before May 2019. Climatic conditions and population activity are different. Seasonal effects are often considered by comparison of the previous year at the same period, but the four centres did not participate in the France PCI registry before 1st May. The period after the fire was not extended to the year 2020 because of the coronavirus disease 2019 (COVID-19) pandemic. In fact, various studies have shown an impact of the pandemic on hospitalizations for myocardial infarction. The decrease in admissions for myocardial infarction during the period of the first lockdown in France is estimated at 30% [13]. Despite this, we made the methodological effort to consider a possible seasonal effect by adjusting the results of the city of Rouen on the city of Le Havre. We hypothesized that the seasonal effect, as well as potential events that could influence the number of events, was parallel between the two cities. Although the distance between the two cities is only 100 km, the city of Le Havre may not be a good control. Indeed, Le Havre is also a very industrialized city, with many polluting factories whose activity can vary over certain periods, such as July and August. A post hoc analysis was performed with correction of the seasonal effect based on paired differences in the same city in 2019 compared with 2020; unfortunately, the effect of the COVID-19 pandemic may have biased the data in 2020. This bias is not maximal, as the study period

(May 2020 to December 2020) was quite a calm period for the COVID-19 pandemic in France, with no lockdown in this period. Moreover, we did not observe a reduction in the number of coronary events in 2020 compared with 2019.

Second, as only patients who had coronary angiography were included, the real number of cases may be underestimated; this bias is not necessarily different between periods. On the other hand, it is possible that the fire also had an impact on other localizations of atherosclerotic disease (such as stroke, acute limb ischaemia) not evaluated in this study.

Finally, we were unable to measure the level of air pollution during the period studied. Air pollution induced by the Lubrizol fire is a complex variable to study. Many different compounds spread through the air, many of which could not be measured directly, with a heterogeneous dispersion. Air pollution measurements are carried out by Atmo Normandie, and are available on a dedicated website (www.atmonormandie.fr). Atmo Normandie published a daily air quality index, but its calculation does not consider odours or atypical pollutants emitted during accidents such as the Lubrizol fire in Rouen. Furthermore, the measurement stations taken into account in the calculation of the Rouen index are not located in the path of the plume of smoke, and the measurements were temporally suspended on the day of the fire. Air samples taken on the day of the fire by the firefighters showed concentrations below the reference values for short-term health risks, except for those taken at the Lubrizol site. Apart from odour nuisance reported by the population, Atmo Normandie did not observe any overrun of the regulatory thresholds on its measurement network in the following days. On the other hand, the level of air pollution in the 112 municipalities exposed to the smoke plume may also be non-uniform.

Conclusions

Our study did not find a significant increase in the incidence of acute and overall coronary events after the Lubrizol fire in Rouen. However, studies of the toxicity of fine particles resulting from combustion lead us to remain cautious when faced with such industrial accidents. Similar studies and longer-term follow-up of exposed patients are needed to further assess their impact.

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Disclosure of interest

The authors declare that they have no competing interest.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at https://doi.org/10.1016/j.acvd.2022.05.003.

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