ORIGINAL ARTICLE

Use of fresh-frozen plasma in 2012 at the Fondazione Ca' Granda Hospital of Milan: assessment of appropriateness using record linkage techniques applied to data routinely recorded in various hospital information systems

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Background. The Quality Unit of a research and teaching hospital in Milan assessed the increased clinical use of fresh-frozen plasma in patients treated during 2012 in order to evaluate the appropriateness of this use.

Materials and methods. For each patient in the study, a pathology profile was generated by means of record linkage techniques involving data collected through different information systems. Patients' information was combined using the patient identifier key generating pathology profiles exported to an Excel file. The profiles were reviewed by two haematologists who identified 101 potentially inappropriate treatments for which the medical records had to be reviewed manually.

Results. In 2012, 490 patients were transfused and for 473 cases the automatic record linkage provided a complete profile. The information relating to the remaining patients did not match, mainly because the patients underwent outpatient procedures for which clinical information is not automatically recorded. In the overall audit only 13 treatments were judged inappropriate.

Discussion. Our study supports the view that record linkage techniques applied to data routinely recorded in different hospital information systems could be potentially extended to support clinical audits, enabling the generation of automated patient profiles that can be easily evaluated, relegating manual checks on medical records to doubtful cases only. Moreover, the method applied in this study allows the analysis of a full set of cases instead of sample surveys, increasing the robustness of the audit results.

Keywords: plasma, clinical governance assessment, health information systems, record linkage, pharmacoepidemiology.

Introduction

Plasma is a blood component that can be derived from whole blood by separation or plasmapheresis. The resulting fresh plasma is frozen within given time limits at temperatures that can adequately preserve the activity and the quantity of the labile coagulation factors[1].

In Italy, the Blood System is run under a public governance scheme[2]. The Italian National Blood Centre is the competent authority that coordinates and supervises the 21 Regional Blood Transfusion Centres with the aim of guaranteeing homogeneous standards of quality and safety across the 310 exclusively public and hospital-based blood establishments. Blood is collected only from voluntary and non-remunerated donors. One of the goals of the Blood System is to reach national self-sufficiency for blood, blood components and plasma-derived medicines (i.e., albumin, coagulation factors and immunoglobulins). Regions send the plasma collected by blood establishments, and not used for transfusion purposes, to authorised manufacturers that produce plasma-derived medicines under a toll fractionation agreement. Regions retain ownership/property of the raw materials and the equivalent derived products throughout the whole process. Both the management and control of the production process and the distribution of plasma for third-party processing are carried out by Regional Blood Transfusion Centres. If the amount of plasma collected remains constant but the plasma needs for clinical use increase, the quantity of plasma available for toll fractionation and production of plasma-derived medicines decreases and hospitals are therefore compelled to increase their intake of plasma-derived medicines bought on the free market, normally at greater cost[3-5].

Fresh-frozen plasma (FFP) is the most misused blood component in the clinical setting[6-9]. Until the 1990s this led to an unjustified exposure of patients to the risk of contracting viral infections[3-6]. However, the introduction of new screening tests including nucleic acid amplification tests, has significantly mitigated this risk. Currently, therefore, the major clinical risks of plasma use

are severe transfusion reactions such as allergic reactions, transfusion-related acute lung injury and transfusion-associated circulatory overload and excessive use of plasma would mainly translate into economic damage.

The *Fondazione Istituto di Ricovero e Cura a Carattere Scientifico Ca' Granda Ospedale Maggiore Policlinico* (*Fondazione* hereafter) is a research and teaching hospital in Milan. It has three emergency units (adult, paediatric and obstetric), kidney, liver, lung, cornea and bone marrow transplant centres, a Medical School, several post-graduate schools and some three-year courses for healthcare providers of the Faculty of Medicine and Surgery of the University of Milan. It also hosts a training centre for postgraduate courses and first and second level Master's Degrees.

During 2012, the *Fondazione* was obliged to purchase immunoglobulins on the market because the hospital Transfusion Centre had been unable to send a quantity of plasma for fractionation sufficient to meet the needs for the finished product.

Therefore, during 2013, the strategic management leadership of the *Fondazione* carried out an assessment of FFP use and its effect on drug costs. The scope of this exercise was two-fold: to obtain sufficient information to enable clinical governance measures to be taken if inappropriate use was discovered or, if FFP uses proved to be justified, to revise the blood donor programmes.

Italian and foreign guidelines on the appropriate use of plasma identify correct/incorrect usage areas as shown in Table I[1-6,10-20]. Nevertheless, composition and properties of plasma make its inappropriate use quite likely, especially when treating the clinical conditions shown in the second part of Table I. Such an inappropriate use does not necessarily compromise the effectiveness of the treatment provided, but it may negatively affect the efficient use of resources within the healthcare system. In fact, whenever plasma use has been identified as inappropriate, there is an equally effective therapeutic treatment at a lower cost: for instance, the use of pharmaceutical products containing the single coagulation factors the patient needs, prothrombin complex concentrates or vitamin K, rather than plasma expanders[21,22].

During the 1990s the Transfusion Centre of the *Fondazione* set up a process of computer-aided auditing[7,8], but this activity had to be discontinued following the introduction of regional software which did not envisage it.

In order to review plasma uses, it would have been quite impractical to conduct a systematic review by evaluating manually every medical record of every patient who had received a FFP transfusion. For this reason, it was decided to set up a record linkage[23,24] strategy aimed at automatically defining a "pathology profile" of the patients treated. Then, appropriateness of FFP use was first assessed through the examination of these profiles, with integration from medical records if needed, by two haematologists assigned to the Transfusion Centre.

Generally speaking, record linkage techniques allow data integration, identifying and matching individual records that refer to the same entities from disparate databases. This paper focuses on the analytical methods adopted and the results obtained through the record linkage of information routinely recorded on different information systems in the *Fondazione* concerning the same patient and shows the potentialities of record linkage for clinical governance programmes.

No ethical approval was needed for the study according to regional law 24/12/2012 n. 3, which allows the data analysis of hospital medical records for quality and appropriateness evaluation programmes.

Materials and methods

Guidelines and evidence published in the literature

The Italian Transfusion System already provides several guidelines on FFP use drawn up by Italian, European[1-6,10-16,20] and international[17-19] societies. Moreover, in many Italian hospitals the committees for the proper use of blood have defined internal protocols[25-28]. All guidelines agree in describing as appropriate the FFP use under the pathological conditions shown in the upper section of Table I, while its use in the clinical conditions shown in the lower section is deemed inappropriate since other valid therapeutic options exist for such cases[29-34].

Data entry and hospital information systems

Information considered necessary for the assessment included: (i) patients' characteristics; (ii) period of hospitalisation and of provision of FFP transfusion including the number of units transfused; (iii) primary and secondary diagnoses at the moment of discharge, with indication of all invasive medical and surgical procedures performed during the period considered; and (iv) blood tests performed throughout the period spent in hospital. The laboratory tests assessed in order to define the appropriateness or inappropriateness of FFP transfusion were, in particular, those concerning the patient's coagulation status, such as prothrombin time (PT) and its Normalised Ratio, activated thromboplastin time (APTT) and its Normalised Ratio, and the levels of fibrinogen, fibrinogen degradation products/D-dimer, protein S, protein C and antithrombin III.

In order to define a patient's pathology profile (PPP), information had to be retrieved from various hospital information systems (Table II):

- EMONET (Insiel Mercato SpA, Trieste, Italy): an information system of the Transfusion Centre which manages the whole workflow of a single

blood component unit from the blood collection of the donor to the transfusion to the patient. This information system is widely used in Italy and is the reference system for the Regional Health Authority.
- ACCENET (Hi.Tech Software Engineering SpA, Bagno a Ripoli, Italy): an information system in which all the characteristics of every hospital admission are registered collecting variables from the Hospital Discharge Module (SDO in Italian), the summary of every hospital medical record. The variables collected are defined by the Ministry of Health and the Regional Health Authority for systematic data collection for epidemiological and economic (hospital payment) purposes.
- CUPNET (Hi.Tech Software Engineering SpA): an information system in which all the services in the outpatient setting are registered. The variables collected are defined by the Ministry of Health and the Regional Health Authority for systematic data collection mainly for economic purposes (hospital payment) and contain only generic descriptions of the activities performed, without reporting patients' conditions.
- CONCERTO (Dedalus Healtcare Systems Group SpA, Firenze, Italy): the information system of the Laboratory Department which manages the whole workflow of a single laboratory test from the medical request (internal or external to the hospital) to the laboratory report. Some of the variables collected are defined by the Ministry of Health and the Regional Health Authority for systematic data collection for economic purposes (hospital payment).

Table I - Use of FFP deemed appropriate/inappropriate and criteria for assessment.

Appropriate use of FFP	
Disease	*Selection criteria*
Congenital or acquired deficiencies of single coagulation factors	- If the specific concentrate is NOT available (e.g. factors V and XI). - If bleeding is ongoing or for bleeding prevention in case of surgery or invasive procedures.
Acquired deficiency of multiple coagulation factors	- If PT or APPT ratios >1.5. - If bleeding is ongoing or in case of significant bleeding risk associated with surgery or invasive procedures.
Severe liver disease	- If bleeding is ongoing. - For bleeding prevention in case of surgery or invasive procedures.
Vitamin K deficiency or on vitamin K antagonist therapy	- If prothrombin complex concentrate is not readily available (first-choice treatment). - In case of intracranial or severe bleeding. - In preparation for not deferrable surgery.
Acute disseminated intravascular coagulation	- If bleeding is ongoing or in association with correction of the underlying cause.
Microvascular bleeding	- In case of massive transfusion after trauma or surgical manoeuvre.
Thrombotic microangiopathy (thrombotic thrombocytopenic purpura, haemolytic uraemic syndrome, haemolysis, elevated liver enzymes and low platelet count - HELLP)	- As substitution fluid.
Hereditary angioedema due to C1-esterase inhibitor deficiency	- If the specific C1-inhibitor plasma derivative is not available.
Whole blood reconstitution for exchange transfusion	
Neonates with congenital deficiencies of single coagulation factors	- If the specific concentrate is NOT available.
Neonates with deficiency of vitamin K-dependent coagulation factors	- If bleeding is ongoing and/or in case of invasive procedure if the specific concentrate is NOT available.
Neonates with disseminated intravascular coagulation	- If bleeding in ongoing or in association with correction of the underlying cause.
Neonates with severe coagulopathy	- In case of bleeding risk (pre-term infants at gestational age ≤28 weeks and/or intubated with previous intraventricular haemorrhage for 48/72 hours). - In case of invasive procedure.
Contraindications	
Congenital IgA deficiency with anti-IgA antibodies in adults	
Inappropriate aims of treatment	
Use as plasma expander	
Treatment of hypoproteinaemia	
Treatment of immunosuppression	
Nutritional purposes	
Treatment of haemostasis disorders in chronic liver disease not complicated by haemorrhage	

PT: prothrombin time; APTT: activated partial thromboplastin time; Ig: immunoglobulin.

Table II - Information needed to generate a patient's pathology profile (PPP) from the hospital information systems and selected variables.

Type of variables needed in PPP	Name of information system	Selected variables
Selection of blood component	EMONET	**Surname, name, gender, date of birth (*IDpat.*)**, date of request, request form ID, applicant ward, type of request, blood component ID, delivery date, delivery ward, single ID code of the blood component unit. Variable that defines the first subset of data; **blood component ID=FFP**
Pathological conditions of the patient and procedures performed during hospitalisation	ACCENET	Admission ID, type of activity (standard/day hospital), **patient ID**, date of admission, date of discharge Diagnosis IDs (max 6 diagnoses ICD9-CM), date and surgery/procedure ID (max 6 procedures ICD9-CM), type of discharge, ID of units in which the patient was admitted during the hospitalisation. Variable that defines the first subset of data; **patient ID = *IDpat identified in EMONET selection***
Type of treatment given to the patient in an outpatient setting	CUPNET	**Patient ID**, outpatient treatment, date of outpatient treatment. Variable that defines the first subset of data; **patient ID = *IDpat identified in EMONET selection***
Results from coagulation-related blood tests	CONCERTO	**Patient ID**, date of request, request ID, applicant ward, request test ID, test result ID, result value. Variable that defines the first subset of data; **patient ID = *IDpat identified in EMONET selection***

The variables used for record linkage are shown in **bold type.**
FFP: fresh-frozen plasma.

Record linkage and construction of patients' pathology profiles

The linkage of the variables collected in the different information systems on the same patient was achieved through the patient's tax code which is the unique patient identifier used in the National Health System in Italy. It consists of 16 characters (both digits and letters) and is assigned to everyone born in Italy and to every immigrant by the Inland Revenue Agency. It is formulated by means of an algorithm[35] that takes into account the individual's name, surname and date and place of birth. The tax code was not present in one of the information systems, EMONET, but, given the availability of some of the required information it was possible to apply the algorithm used for its calculation and thereby automatically generate the first 11 characters of the tax code. The link between the variables recorded in the transfusion system and the remaining systems was therefore made using just the first 11 digits of the tax code (ID). After verification that truncation never produced coincident 11-character truncations of different patients' 16-character tax codes, no ambiguity in the assignment of the data selected for each PPP was found, and record linkage resulted fully deterministic.

Since the first selection of the records in the different information systems was made using only the patient's ID, the records retrieved did not necessarily all refer to the same hospital admission. In order to obtain a profile of the patient on the basis of each individual hospital treatment, time consistency was checked as shown in Figure 1. Record linkage was then performed by subsequent iterations: (i) all FFP units assigned (EMONET) during each hospital stay were identified by retrieving recipient patients from 2012 and 2013 hospitalisation databases (ACCENET) in order to identify any FFP unit assigned in 2012 during hospital stays begun in 2012 and ended in 2012 or 2013; (ii) recipient patients were sought among outpatients' ward records (CUPNET) for all FFP units not assigned during hospital stays. In a second phase, coagulation tests were selected in CONCERTO by linking the patient's ID with consistent dates of laboratory tests, admission and assignment of FFP units. At the end of the record linkage procedure, each FFP unit assigned during 2012 was identified and linked to a treatment provided to a patient.

The information selected from each information system was then converted into text file format and loaded into an ACCESS 2007 format database. Using ACCESS the data were processed and the PPP generated were exported into Excel format and anonymously provided to the clinicians.

Finally, a PPP was generated for all patients for whom hospital treatment and/or blood test parameters had been identified. An example of a PPP is shown in Figure 2.

Assessment of the appropriateness of use of fresh-frozen plasma

Two haematologists reviewed the PPP, identifying potentially inappropriate treatments. If the two reviewers

did not agree, the evaluation of a third senior medical doctor of the Transfusion Centre was required. The patients' medical records were manually read only in cases in which: (i) assessment of a PPP did not enable an opinion on the appropriate use of FFP; (ii) information on the patient's coagulation status was lacking; (iii) an unusual pathology was encountered; or (iv) the doses of FFP transfused appeared insufficient.

It was decided not to proceed with the record linkage method to assess the appropriateness of transfusions in neonatal cases for various reasons. In particular, coagulation times in neonates are longer on average

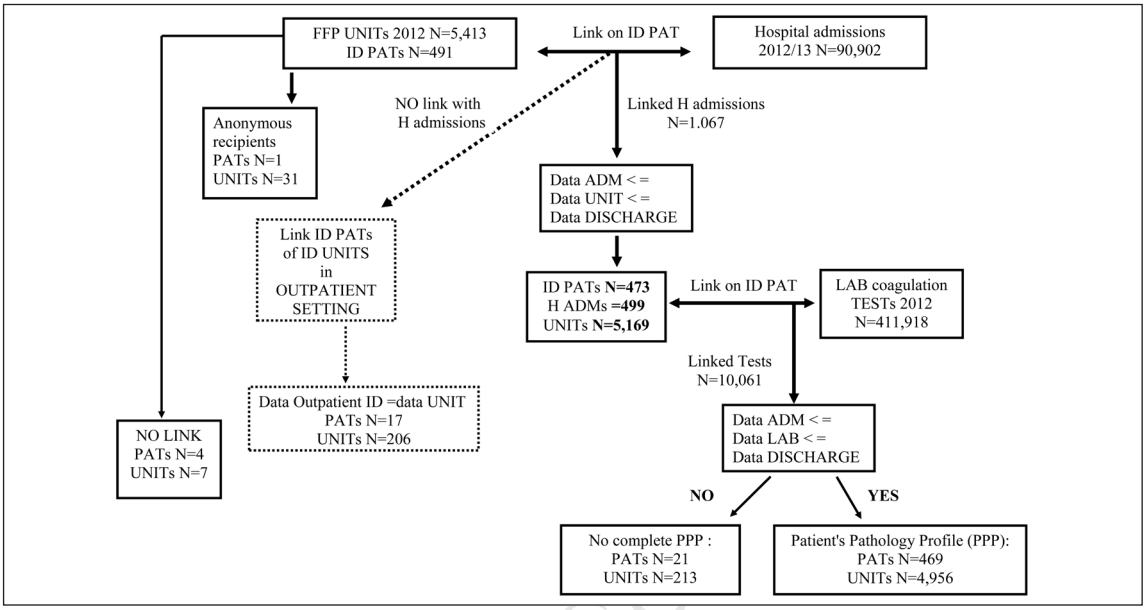

Figure 1 - Record linkage algorithm for the generation of patients' pathology profiles (PPP).
FFP: fresh-frozen plasma; ID PAT: patient identification code; PATs: patients; UNIT: unit of fresh-frozen plasma; Data ADM: data of hospital admission; Data UNIT: data of transfusion of the fresh-frozen plasma unit; Data LAB: data of laboratory test request; Data DISCHARGE: data of discharge; Data Outpatient ID: data of outpatient treatments; H ADM: hospital admission.

ID PAZ	DT LAB	ID RIC LAB	PT SEC	PT RATIO	APTT SEC	APTT RATIO	D DIMER	FIBRINOGEN
U3	20-Jan-12	25573289	29.2	2.81	41.9	1.33		
	20-Jan-12	25573293	22.2	2.13	42.8	1.36		
	20-Jan-12	25573296	22.3	2.14	57.1	1.82		

ID PAZ	SEX	AGE	ADM DT	ID HOSP	TYPE HOSP	N BAGS	DISC DT	DIAGN 1	DIAGN 2	DIAGN 3	DIAGN 4	DIAGN 5	DIAGN 6	DT INT 1	INT 1	DT INT 2	INT 2	DT INT 3	INT 3	DT INT 4	INT 4	DT INT 5	INT 5	DT INT 6	INT 6
U3	M	49	20-Jan-12	2012003340	URGENT	6	20-Jan-12	RESPIRATORY INSUFFIC.	HAEMATEMESIS	ANOTHER SHOCK WITHOUT MENTION OF TRAUMA	ALCOHOLIC LIVER CIRRHOSIS	INFEROLA-TERAL MYOCARDIAL INFARCTION, INITIAL EPISODE OF CARE		20-Jan-12	MECHANICAL VENTILATION FOR LESS THAN 96 HOURS IN SUCCESSION	20-Jan-12	SOFT BOWEL ENDOSCOPY	20-Jan-12	COMPUTERISED AXIAL TOMOGRAPHY (CAT) CHEST	20-Jan-12	COMPUTERISED AXIAL TOMOGRAPHY (CAT) ABDOMEN				

Figure 2 - Example of a patient's pathology profile (PPP).
ID PAZ: identification code of the patient in the study; DT LAB: date of laboratory request; ID RIC LAB: identification code of laboratory request; PT SEC: prothrombine time; PT RATIO: prothrombine time standardised ratio; APTT SEC: activated partial thromboplastin time; APTT RATIO: partial tromboplastin time standardised ratio; ID_HOSP: identification code of the hospitalisation; ADM DT: date of admission for hospitalisation; TYPE HOSP: type of hospitalisation; N BAGS: number of units transfused; DISC DT: date of discharge; DIAGN 1-6: ICD9-CM codes of diagnoses 1 to 6; DT INT1-6: dates of interventions from 1 to 6; INT 1-6: ICD9-CM codes of interventions from 1 to 6.

than those of adults and not necessary linked to bleeding risk. This is even more true in case of preterm infants in whom abnormalities in the coagulation tests, unless they are particularly significant, and in the absence of symptoms or bleeding risk, do not represent an indication for an FFP transfusion. With premature babies, the complex clinical picture and the impossibility of performing daily blood tests leads the record linkage method to lack information indispensable to define the appropriateness of the FFP transfusion. In these cases, the appropriateness of the FFP transfusion could only be assessed by a conventional review of the medical records. For this reason the description of neonatal cases in Table III and the first section of the Table SI reported in the online supplementary content, which summarises the distribution of Diagnosis-Related Groups and the main diagnoses relating to the 78 neonatal cases, is shown only as an illustration of the cases dealt with in our Transfusion Centre. These cases were not included in the final assessment.

Results

During 2012 the Transfusion Centre of *Fondazione* assigned 5,413 units of plasma, of which 5,382 to non-anonymous recipients. Recipients are defined as anonymous in the rare cases they are admitted to the emergency unit without ID documents or when it was necessary to give the transfusion before they had been identified. The 5,382 units transfused to correctly identified subjects corresponded to 1,167 requests for a total of 490 patients in 521 hospital admissions or outpatient treatments (some patients received more than one treatment during the year analysed).

Using the analytical method proposed it was possible to extrapolate, rapidly, plenty of information concerning the patients and their clinical workflow from the various information systems. First of all it was possible to collect statistical data on patients' population (gender, age), the number of requests for FFP, the number of units transfused, the level of care (hospitalisation or emergency unit). This provided a synthetic description of the characteristics of the patients analysed (adults/children) and the settings in which the FFP units had been used (medical/surgical or emergency unit) (Table III).

Moreover, it was possible to extrapolate the clinical characteristics of the patients analysed. The table reported in the online supplementary material shows the distributions of the Diagnosis-Related Groups and the main diagnoses relating to the hospital treatments for 78 neonatal patients, 14 patients aged under 14 and 403 adult patients who could be assessed on the basis of their hospital information. Patients aged under 14 are conventionally classified as paediatric and are treated in paediatric wards, which is the reason why they are assessed separately from the adult cases; the criteria for judging plasma transfusion are nevertheless the same as those applied to adult patients.

Lastly, it was possible to assess the workload distribution between the various operative units showing that the departments mainly requesting and transfusing FFP are the liver transplant centres, and the surgical, intensive care and resuscitation units. This is confirmed by the data analysed for appropriateness.

Analysis of the information collected enabled a judgment on appropriateness of FFP. The subjects assessed, on the basis of the pathological conditions deemed suitable for FFP transfusion (Table I), are summarised in Table IV.

Following the analysis of treatment given to adult patients, FFP use appeared appropriate in 302 cases simply on the basis of the consistency of the information shown in the PPP. A manual review of the paper medical records was necessary in the remaining 101 cases, either because the information in the PPP was not considered sufficient to express a judgment on appropriateness (n=86), or because the profile indicated an inappropriate use that nevertheless required confirmation (n=15).

Table III - Characteristics of the patients and the setting of FFP requests identified through record linkage.

Type of patient	Setting	N. of treatments	Gender	Average age (SD)	N. of FFP requests	N. of units
Children (≤age 14)	Hospitalisation	92	M=54, F=38	Neonates 78 (0; 0) 14 others (7.9; 4)	206	256
	Outpatient unit	4	M=4	6.5; 5.2	23	58
	Unknown	3	M=1, F=2	2 age=0; 1 age=13	4	4
Adult (>age 14)	Hospitalisation	407*	M=211, F=196	57.6; 17.3	901	4,913
	Outpatient unit	14	M=10, F=4	49.6; 23.5	32	148
	Unknown	1	M=1	49	1	3
Total		521	M=281, F=240	46.7; 27.0	1,167	5,382

* No discharge data are available for four hospitalised subjects. SD: standard deviation; FFP: fresh-frozen plasma.

Table IV - Distribution of adult patients assessed in relation to the pathological conditions for which use of fresh-frozen plasma is deemed appropriate.

Pathological condition	Cases
Correction of congenital or acquired deficiencies of single coagulation factors	3
Correction of acquired deficiencies of multiple coagulation factors	130
Severe liver disease	140
Acute disseminated intravascular coagulation	7
Correction of microvascular bleeding	114
Apheresis in thrombotic microangiopathies (thrombotic thrombocytopenic purpura, haemolytic uraemic syndrome, haemolysis, elevated liver enzymes and low platelet count - HELLP)	9

At the end of the assessment of the medical records, 13 patients proved to have received inappropriate transfusion of FFP (3.2%). Tests showed that these patients' coagulation was within normal limits but without haemorrhagic diathesis such as to justify transfusion. Moreover, in four cases appropriateness criteria were met but the quantity of plasma transfused proved insufficient given that a single unit of plasma had been transfused. This was insufficient in relation to the patients' weight, as obtained from the medical records.

Given that information on patients' height and weight could not be obtained from the information systems, in the 302 cases for which the medical records were not analysed, the general rule was applied that one unit of plasma was to be considered insufficient while the transfusion of two or more units was appropriate.

For two treatments judged inappropriate and for one treatment judged appropriate the third opinion of the senior reviewer was needed.

In conclusion, the results of our study have demonstrated that about 97% of the plasma use in *Fondazione* was in line with internal guidelines, which, in turn, were drawn up on the basis of national and international guidelines.

Discussion

The potentiality of the "record linkage" analytical method was exploited to set up a systematic review of all the plasma transfused during the year 2012.

Using the demographic, clinical and laboratory information about patients, summarised in the PPP, it was possible to assess the laboratory tests performed on the days on which a patient received a FFP transfusion and in the following days. These were also associated with any information relating to surgical or invasive procedures performed during the same hospital admission. It was then possible to assess the appropriateness or inappropriateness of the FFP transfusions administered.

The very high level of appropriateness found, higher than the levels emerging from the literature[36-41], can be explained by various factors. In the first place, the departments of the *Fondazione* that mainly request FFP are surgical, intensive care, emergency, resuscitation units and, especially, the liver transplant centre. This last, in particular, admits patients who often have a clear necessity for FFP transfusions taking into account their primary disease, clinical picture or surgery needed. Secondly, the *Fondazione* had set up computerised audit activities over the years[4,5], together with continuous updating of internal protocols[28]. Both of these are valid guides for the departments and for correct clinical practice. Last but not least, the ongoing collaboration with colleagues at the Coagulation Centre has ensured a readily available advisory service. This has undoubtedly contributed greatly to appropriate handling of transfusion requests by the various departments.

In this way, the strategic management leadership of the *Fondazione* was fully assured that the use of FFP was appropriate and that the increased use of plasma transfusions complied with the hospital's protocols and best practices. It is, therefore, possible to conclude that the smaller amount of plasma sent to industry for fractionation was not caused by inappropriate use of FFP but was justified by increased clinical needs.

The record linkage system also enabled a comprehensive overview of the activities of our Transfusion Centre and, especially, of its single departments, resulting in an assessment of the workload distribution and the transfusion requests.

Nevertheless, certain limits emerged, especially with regards to premature neonates, for whom careful examination of the paper medical records is still required on account of the clinical complexities, and also because of the difficulty of obtaining computerised information on blood tests that are not performed routinely in this population of patients.

Other limits to this analytical system derive from the fact that, as of now, data referring to outpatients' treatment are not sufficiently computerised to enable assessment of these patients. As described in the literature, an analysis of the appropriateness of plasma transfusion is also expected to take into account the patient's weight, a variable that is not presently retrievable from the information systems of the *Fondazione*[36-41].

From a data management point of view, the analysis revealed that the various laboratories collaborating with the central laboratory do not use the same patient identification codes. This makes it more difficult to retrieve all the information regarding a given period and to perform the record linkage for a given patient if there is a lack of information at the central laboratory. Harmonisation of patients' identification

codes throughout the secondary information systems of the *Fondazione* is certainly an area for the future improvement of this analytical system.

Conclusions

The "record linkage" analytical method, which assembles information regarding each single patient from several data sources, proved to be very rapid since a great deal of information was retrieved from the hospital information systems alone. It was also efficient since it enabled analysis of a wider range of cases than other methods and, lastly, it was effective since the manual review of the medical records, aimed at retrieving the few, well-identified data not contained in the computerised profiles, was necessary for only 25% of the entire population receiving transfusions.

In spite of the limits stated in the discussion, record linkage remains an extremely valid and efficient system for assessing activities, since it enables analysis of a wide range of cases and, notwithstanding the lack of certain data (e.g. the patient's weight), allows the assessment of the appropriateness of FFP transfusion on a prevalently clinical basis.

The assessment described paved the way to further audit programs using record linkage techniques to produce a huge factual base for clinical and organisational improvements.

Authorship contributions

ML and SC designed the research study and wrote the paper; ML analysed the data; BO and AA reviewed the medical charts, and ER and MM reviewed the clinical aspects of the analysis.

All the Authors approved the final version of the paper.

The Authors declare no conflicts of interest.

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